

How to Cite:

Aithal, R. R., Malavika, M., Pejawar, S. R., & Parthasarathy, P. (2022). Comparison of three doses of intrathecal fentanyl (15 mcg, 20 mcg and 25 mcg) for labour analgesia. *International Journal of Health Sciences*, 6(S2), 12635–12654.
<https://doi.org/10.53730/ijhs.v6nS2.8383>

Comparison of three doses of intrathecal fentanyl (15 mcg, 20 mcg and 25 mcg) for labour analgesia

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Abstract---Background and Objectives: Intrathecal fentanyl provides rapid profound analgesia in labouring parturients in the dose range of 10-50 mcg. Therefore, this study was taken up to compare the effects of three different doses of intrathecal fentanyl (15mcg, 20mcg and 25mcg) with regards to onset and duration of analgesia and to find the effective and safe dosage of the drug for labour analgesia. Materials and Methods: A comparative double blinded RCT was performed on 90 term multigravida parturients after obtaining approval from Institutional Ethical Committee. They were divided randomly into three groups (Groups A, B and C) with 30 parturients each. At cervical dilatation of 3-5cm, they received intrathecal fentanyl 15mcg, 20mcg or 25mcg respectively. In all groups, variables such as HR, SBP, DBP and MBP, SpO₂, pain assessment by VAS and sedation score by RSS were recorded at different points during the course of labour and mode of delivery and APGAR score was noted after the delivery of the baby. Results: The demographic data was comparable between the groups. The mean duration of onset of analgesia was 13+/-1 min, 9+/-1min and 5+/-1 min in groups A, B and C respectively. The mean duration of analgesia in groups A, B and C respectively were 56+/-

2.5min, 73.5+/- 4.4min and 89.4+/-3.2min. The duration of labour, mode of delivery, birth-weight, APGAR scores at 1minute and 5minutes and NICU admission rates were comparable between the groups. Among the groups, 2 parturients in group A (6.7%), 4 in group B (13.3%) and 8 in group C (26.7%) experienced pruritus, but was not statistically significant. Conclusion: In our study, 20mcg and 25mcg intrathecal fentanyl proved to be effective dosages in multigravida parturients for labour analgesia compared to 15mcg intrathecal fentanyl with respect to onset and duration of analgesia and had no effects on neonate. The dosage of 20mcg intrathecal fentanyl was safer than 25mcg intrathecal fentanyl due to fewer incidences of side effects like pruritus.

Keywords---obstetric anaesthesia, labour pain, labour analgesia, opioids, subarachnoid.

Introduction

Labour pain is a unique pain associated with a very special event in a woman's life- the birth of a baby. Through the passing years, many methods have been used to relieve the pain of labour and make the process of labour a smooth one. Maternal and fetal wellbeing may be affected by maternal physiological responses to labour pain. Hence, providing effective and safe analgesia during labour is an ongoing challenge. Single subarachnoid injection for labour analgesia is easier to initiate, effective and rapid, compared with epidural analgesia. The advantage of regional analgesia compared with systemic opioids and inhaled anaesthetic is higher quality pain control, decreased adverse fetal effects.¹ Large surveys investigating the combined spinal-epidural (CSE) technique have shown it to be safe and effective with faster onset of analgesia and less motor blockade.^{2,3}

Although local anaesthetic blockade is effective in management of severe pain, it causes vasodilation and hypotension. Lower limb and pelvic muscle power affected, bearing down reflex affected. Since knowledge of nociceptive processes in spinal cord has grown, use of regional analgesia with drugs other than local anaesthetic has increased. Intrathecal opioids like sufentanil and fentanyl have become increasingly popular as intrathecal analgesics for labour.⁴ Intrathecal fentanyl has been reported to provide rapid profound analgesia in labouring patients in the dose range of 10-50 mcg.^{4,5} Previously published studies have found that intrathecal fentanyl provided effective labour analgesia with minimal side effects, in patients in active labour[4,6]. They found that as the dose increased, the duration of analgesia also increased up to certain dose of fentanyl (25 mcg).⁷ Therefore, this study was taken up to compare the effects of three different doses of intrathecal fentanyl (15mcg, 20mcg and 25mcg) with regards to onset and duration of analgesia provided by these doses, to observe for occurrence of any side effects, effects on the newborn, if any and hence, to find the effective and safe dosage of the drug for labour analgesia.

Materials and Methods

Source of Data: Pregnant women admitted to the labour room in Vani Vilas Hospital affiliated to Bangalore Medical College and Research Institute, Bangalore.

Methods Of Collection Of Data

Study design: Comparative double blinded randomized clinical study.

Study period: November, 2016 to May, 2018.

Place of study: Vani Vilas Hospital affiliated to Bangalore Medical College and Research Institute, Bangalore.

Inclusion criteria

1. Pregnant women (multigravida) with no comorbidities (ASA 2- Annexure-1)
2. First stage of labour (spontaneous/ induced).
3. > 18 years of age (willing to give informed consent).
4. Singleton pregnancy with cephalic presentation.
5. Term gestation (37-42 weeks).
6. Back pain assessed by VAS > or equal to 70mm.

Exclusion criteria

1. Patient refusal.
2. Patients who have received analgesics following onset of labour.
3. Multiple pregnancy.
4. Malpresentations.
5. Infection / inflammation at sites of injection/ complications that could cause bleeding (thrombocytopenia).
6. Known allergy to any of the study drugs.

Study Procedure: Following approval of the BMCRI Institutional Ethics Committee and after obtaining informed written consent, 90 parturients were selected and divided randomly with the help of computer generated random number tables in opaque sealed envelopes, into three groups-

GROUP 'A': 15mcg Intrathecal fentanyl group: 30

GROUP 'B': 20mcg Intrathecal fentanyl group: 30

GROUP 'C': 25mcg Intrathecal fentanyl group: 30

A detailed history, complete physical examination and routine investigations of the parturients were done. The study drug was prepared by senior anaesthetist not involved in the procedure. Patients and anaesthesia provider were not aware of the study drug.

Each parturient was hydrated with 500 mL of Ringer lactate solution IV and placed in the left lateral position. The study drug was diluted in normal saline to a total volume of 1mL in all cases. At 3-5cm of cervical dilatation as assessed by the obstetrician, after taking aseptic precautions, L3-L4 intervertebral space was identified and lumbar puncture was done using 25G/26G Quincke Spinal needle.

After clear and free flow of CSF was seen, the study drug was injected intrathecally. The parturient was placed into the supine position with left uterine displacement. Pain scores were recorded immediately before and at 5-min intervals after the intrathecal injection using a 10 cm visual analog score (VAS) (0 mm = no pain, 100 mm = worst pain imaginable (Annexure-2). A mean VAS pain score of 20 was defined to be the highest pain score consistent with adequate analgesia.

The occurrence of the side effects like nausea (N), vomiting (V) and pruritis (P) were assessed at the same times. In the event of vomiting, Inj. Ondansetron 4mg IV was given. If patient complained of pruritis, Inj Chlorpheniramine 10mg IV was given. Sedation was rated by the observer using a Ramsay sedation scale [RSS-Annexure- 2] (1=anxious, 2=cooperative, 3=responding to commands, 4=brisk response to stimulus, 5=sluggish response to stimulus, 6=no response to stimulus) The measurement of the parturients, arterial blood pressure (BP), heart rate (HR), and respiratory rate(RR), arterial oxygen saturation (SpO₂) were performed.

Hypotension was defined as mean arterial blood pressure <60 mm Hg or a 20% decrease from baseline and treated with a fluid bolus and IV ephedrine 6 mg intermittent bolus as required. If HR<50/min, Inj. Atropine 0.6mg IV was given. In the event of respiratory depression (RR<8 or SpO₂<95%), oxygen supplementation and respiratory support were given if required. Sensory level attained was checked by pin-prick method. The maximum level of sensory block and time to attain maximum sensory blockade were noted. Motor block, if any, was assessed by Modified Bromage Score.

Fetal heart rate (FHR) was monitored and FHR of 120–160 bpm was considered normal and baseline variability of ≥6 bpm was considered normal. The Apgar scores of the infant was assessed. All the above parameters were recorded using a preset proforma. Patients were informed that the intrathecal injection might take as long as 15 min to reach its maximum effect. The parturient was permitted to withdraw from the study at any time from the time of enrollment. On request for further analgesia, intravenous fentanyl of 25 mcg was given as rescue analgesia and the patient was managed according to normal clinical routine for the remainder of her labour.

Primary Outcome: Pain Control

Secondary Outcome: Hemodynamic changes, Adverse drug reactions, Effect on the neonate.

Pain was evaluated by Visual Analogue Scale (VAS).

NICU admission if any and the indication for the same were noted.

Progress of labour and fetal heart rate was assessed by the Obstetrician regularly.

Operative intervention: LSCS and indication for the same were also noted.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi- square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Graphical representation of data: MS Excel and MS word was

used to obtain various types of graphs such as bar diagram and line diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyse data.

Sample Size of Estimation: To detect a minimum of 25min difference in duration of analgesia between the three groups, with alpha error of 5% and beta error of 20%, sample size was 30 in each group.

GROUP 'A': 15mcg Intrathecal fentanyl group: 30, GROUP 'B': 20mcg Intrathecal fentanyl group: 30 GROUP 'C': 25mcg Intrathecal fentanyl group: 30

$N = 2(Z_{\alpha/2} + Z_{1-\beta})^2 \sigma^2 / d^2$ where N is the total sample size, $Z_{\alpha/2}$ is the normal deviate at a level of significance (taking 1.96 for 5% level of significance), $Z_{1-\beta}$ is the normal deviate at 1- β % power (taking 0.84 for 80% power), σ is the standard deviation and d is the difference of means.

Results

We enrolled 90 women after obtaining informed written consent. All 90 women fulfilled the inclusion criteria and hence were a part of the study.

GROUP 'A': 15mcg Intrathecal fentanyl group: 30

GROUP 'B': 20mcg Intrathecal fentanyl group: 30

GROUP 'C': 25mcg Intrathecal fentanyl group: 30

They were evaluated for haemodynamic variations, quality of analgesia by visual analogue scale, labour and neonatal outcomes, and side effects if any. We enrolled 90 women after obtaining informed written consent. All 90 women fulfilled the inclusion criteria and hence were a part of the study. GROUP 'A': 15mcg Intrathecal fentanyl group: 30 GROUP 'B': 20mcg Intrathecal fentanyl group: 30 GROUP 'C': 25mcg Intrathecal fentanyl group: 30 They were evaluated for haemodynamic variations, quality of analgesia by visual analogue scale, labour and neonatal outcomes, and side effects if any.

Table 1: Mean age of parturients

	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	25.0	3.8	24.1	2.5	24.0	2.5

The Mean age of parturients was 25 ± 3.8 years, 24.1 ± 2.5 years and 24 ± 2.5 years in Groups A, B and C respectively. There was no significant difference in mean age between the groups ($p=0.4$). ASA grade: The parturients in all the groups belonged to ASA grade 2.

Table 2: ASA grade of parturients

	Group		
	15 mcg Intrathecal fentanyl	20 mcg Intrathecal fentanyl	25mcg Intrathecal fentanyl
ASA grade 2	30 (100%)	30 (100%)	30 (100%)

Anthropometry

Table 3: Mean anthropometric measurements in three groups

	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Height (cm)	152.1	1.7	152.2	1.7	151.9	1.4
Weight (kg)	61.6	1.4	61.4	1.4	61.6	1.6
BMI	26.6	.5	26.6	.6	26.7	.6

The mean heights of parturients in Groups A, B and C were 152.1+/-1.7, 152.2+/-1.7 and 151.9+/-1.4 respectively. The mean weights of parturients in groups A, B and C were 61.6+/-1.4, 61.4+/-1.4 and 61.6+/-1.6 respectively. The mean BMI in Groups A, B and C were 26.6+/-0.5, 26.6+/-0.6 and 26.7+/-0.6 respectively. There was no statistically significant difference between mean height, weight and BMI among the three groups (p=0.9), as these parameters were standardized.

Table 4: VAS before and after analgesia at different intervals of time between the groups

VAS	Group					
	15 mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baseline	91.7	6.5	91.7	6.5	91.7	6.5
5min	75.5	3.8	46.2	4.7	14.5	3.8
10min	46.2	4.7	14.5	3.8	14.5	3.8
15min	14.5	3.8	11.2	2.2	11.2	2.2
20min	11.2	2.2	6.0	4.0	6.0	4.0
25min	6.0	4.0	.5	1.5	.5	1.5
30min	.5	1.5	.5	1.5	.5	1.5
40min	6.7	4.8	6.7	4.8	.5	1.5
50min	11.2	2.2	11.2	2.2	6.7	4.8
60min	16.2	4.7	11.2	2.2	11.2	2.2
80min	39.5	8.4	16.2	4.7	16.2	4.7
100min	56.2	4.7	56.2	4.7	56.2	4.7
120min	72.0	9.2	71.3	9.0	71.3	9.0
140min	78.0	4.1	78.8	5.8	81.5	4.6

160min	87.9	5.7	85.7	5.3	90.7	5.3
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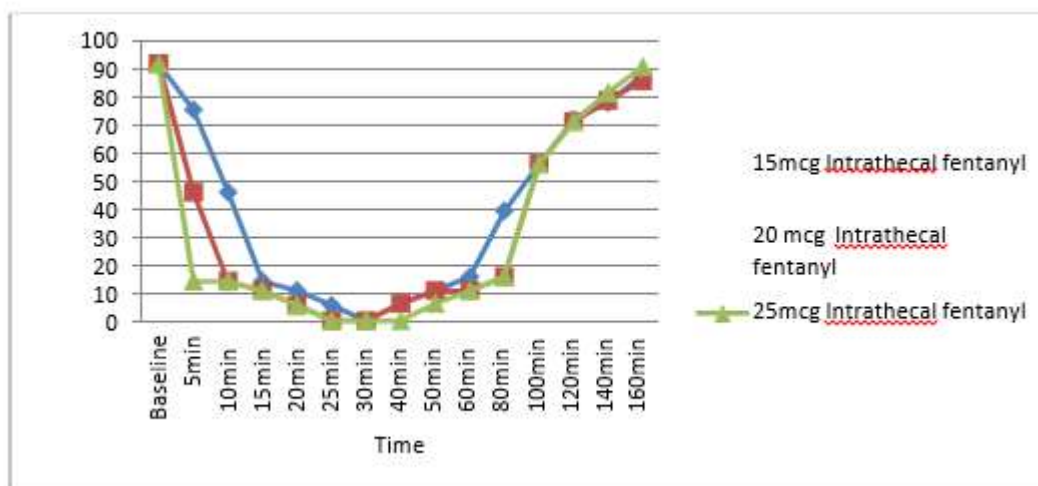


Figure 1: Line diagram showing VAS comparison between the groups

There was significant difference in mean VAS Score between the three groups at all the intervals ($p < 0.0001$) except at baseline and after 100min. The mean VAS scores were higher in Group A compared to groups B and C.

Onset of analgesia

Table 5: Comparison of analgesia onset times between the groups

	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Onset of analgesia min	13	1	9	1	5	1

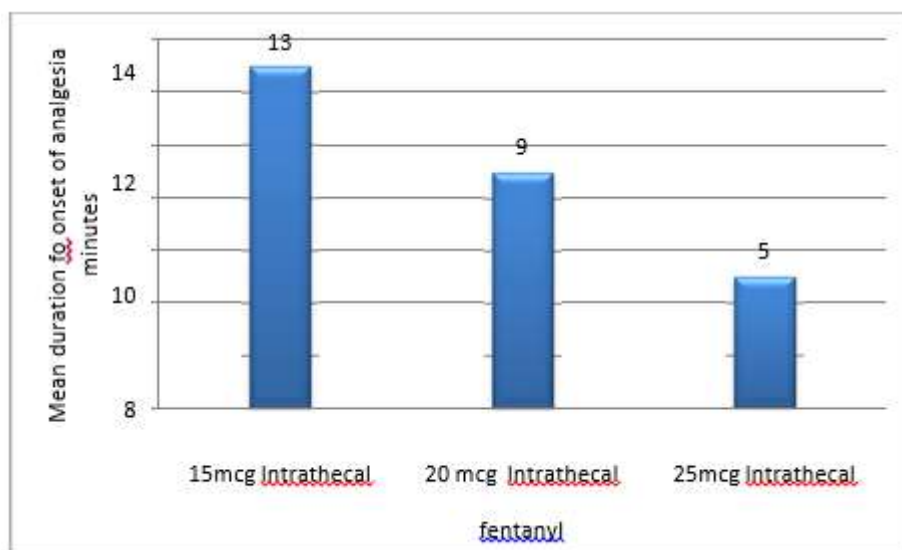


Figure 2: Bar graph showing onset times of analgesia

The mean durations of onset of analgesia were 13+/-1 min, 9+/-1min and 5+/-1 min in groups A, B and C respectively. Onset of analgesia was significantly faster in group C than group B and group A ($p < 0.0001$)

Duration of analgesia

Table 6: Duration of analgesia between the groups

	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Duration of analgesia min	56.0	2.5	73.5	4.4	89.4	3.2

Mean duration of analgesia in groups A, B and C respectively were 56+/-2.5min, 73.5+/- 4.4min and 89.4+/-3.2min. Group C had the longest duration of analgesia compared to groups B and A ($p < 0.0001$).

Rescue analgesia

Table 7: Requirement of rescue analgesia

	Group					
	15 mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	n	%	n	%	n	%

Rescue analgesia	N	19	63.3	27	90.0	30	100.0
	Y	11	36.7	3	10.0	0	.0

Among the groups, 11 patients in group A, 3 in group B and none in group C required administration of rescue analgesia ($p < 0.0001$)

RSS scores

Table 8: Comparison of RSS scores among the groups

RSS	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Baseline	1.00	.00	1.00	.00	1.00	.00
5min	1.00	.00	1.00	.00	2.00	.00
10min	1.00	.00	2.00	.00	2.00	.00
15min	2.00	.00	2.00	.00	2.00	.00
20min	2.00	.00	2.00	.00	2.00	.00
25min	2.00	.00	2.00	.00	2.00	.00
30min	2.00	.00	2.00	.00	2.00	.00
40min	2.00	.00	2.00	.00	2.00	.00
50min	2.00	.00	2.00	.00	2.00	.00
60min	2.00	.00	2.00	.00	2.00	.00
80min	2.00	.00	2.00	.00	2.00	.00
100min	1.00	.00	2.00	.00	2.00	.00
120min	1.00	.00	1.00	.00	1.00	.00
140min	1.00	.00	1.00	.00	1.00	.00
160min	1.00	.00	1.00	.00	1.00	.00

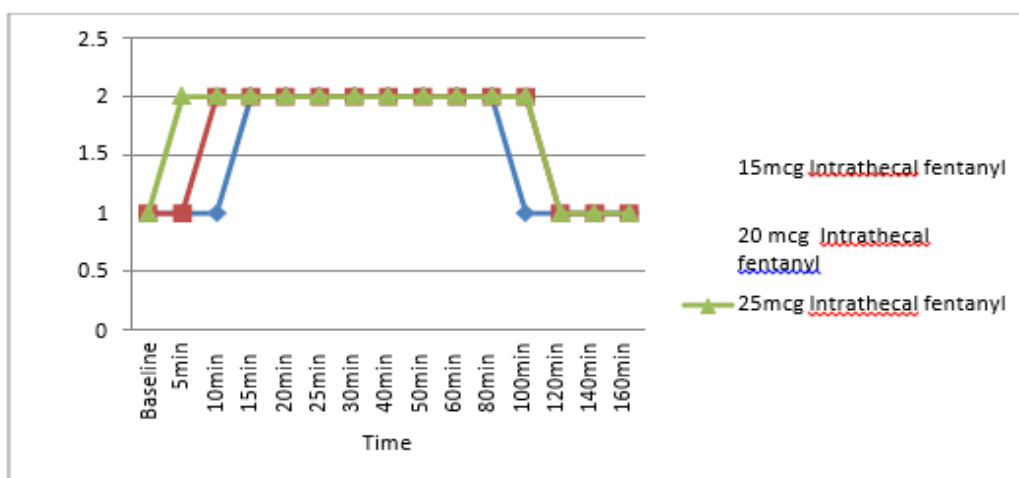


Figure 3: Line diagram showing RSS score comparison between the groups

The time taken to achieve an RSS score of 2 from RSS score 1 in groups A, B and C respectively were 15min, 10min and 5min. In group A, the parturients achieved RSS score of 1 back again faster than in groups B and C.

Sensory level

Table 9: Comparison of sensory levels of blockade attained among the groups

Sensory level		Group					
		15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
		n	%	n	%	n	%
Baseline	Nil	30	100.0	30	100.0	30	100.0
5min	L1	30	100.0	0	.0	0	.0
	T10	0	.0	0	.0	30	100.0
	T12	0	.0	30	100.0	0	.0
10min	T10	0	.0	30	100.0	30	100.0
	T12	30	100.0	0	.0	0	.0
15min	T10	30	100.0	30	100.0	0	.0
	T8	0	.0	0	.0	30	100.0
20min	T10	30	100.0	30	100.0	0	.0
	T8	0	.0	0	.0	30	100.0
25min	T10	30	100.0	30	100.0	30	100.0
30min	T12	30	100.0	30	100.0	30	100.0
40min	T12	30	100.0	30	100.0	30	100.0
50min	L1	30	100.0	30	100.0	30	100.0
60min	L3	30	100.0	30	100.0	30	100.0
80min	L3	0	.0	30	100.0	30	100.0
	S2	30	100.0	0	.0	0	.0
100min	S2	0	.0	30	100.0	30	100.0
	S4	30	100.0	0	.0	0	.0
120min	S4	30	100.0	30	100.0	30	100.0
140min	S4	20	100	20	100	20	100
160min	S4	7	100	7	100	7	100

Table 10: Comparison of maximum sensory levels attained among the groups

		Group					
		15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
		n	%	n	%	n	%
Max sensory level	T10	30	100.0	30	100.0	0	.0
	T8	0	.0	0	.0	30	100.0

Table 11: Time for maximum sensory levels between the groups

	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Time for max sensory level	15	0	10	0	5	0

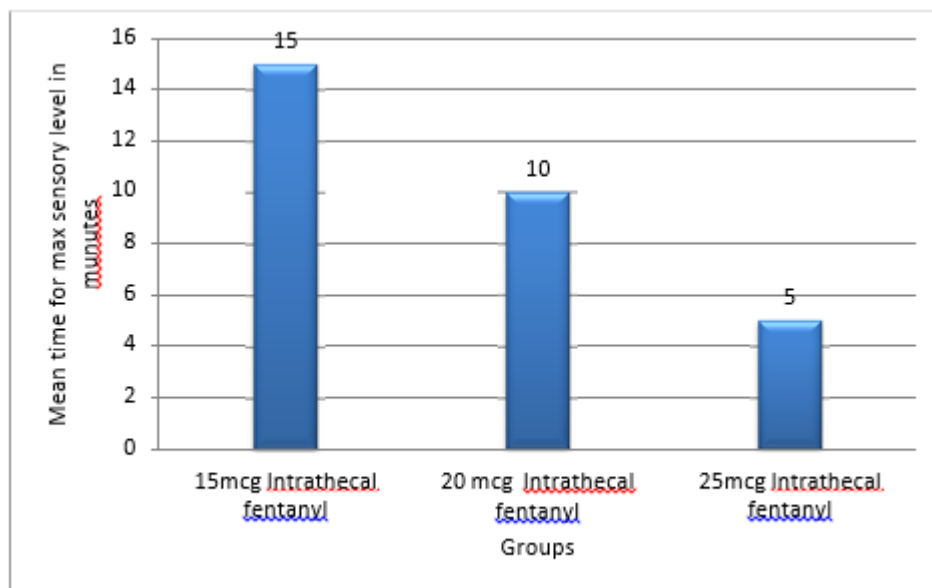


Figure 4: Bar graph showing time for maximum sensory levels

Among the groups, all the subjects in group A and B attained a maximum sensory level of T10 within 15min and 10min respectively. The patients in Group C attained a maximum sensory level of T8 in 5 min ($p < 0.0001$)

Motor blockade

Table 12: Motor blockade comparison between the groups

Motor Block		Group					
		15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
		Count	%	Count	%	Count	%
Baseline	None	30	100.0%	30	100.0%	30	100.0%
5min	None	30	100.0%	30	100.0%	30	100.0%
10min	None	30	100.0%	30	100.0%	30	100.0%
15min	None	30	100.0%	30	100.0%	30	100.0%
20min	None	30	100.0%	30	100.0%	30	100.0%

25min	None	30	100.0%	30	100.0%	30	100.0%
30min	None	30	100.0%	30	100.0%	30	100.0%
40min	None	30	100.0%	30	100.0%	30	100.0%
50min	None	30	100.0%	30	100.0%	30	100.0%
60min	None	30	100.0%	30	100.0%	30	100.0%
80min	None	30	100.0%	30	100.0%	30	100.0%
100min	None	30	100.0%	30	100.0%	30	100.0%
120min	None	30	100.0%	30	100.0%	30	100.0%
140min	None	20	100%	20	100%	20	100%
160min	None	7	100%	7	100%	7	100%

There was no motor blockade seen in any of the three groups at any interval of time after administration of analgesia

Heart rates

Table 13: Comparison of heart rates between the groups

HR/min	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baseline	122.07	6.00	122.13	6.00	122.60	6.23
5min	118.67	4.63	118.67	4.63	119.07	4.60
10min	110.90	3.61	110.77	3.41	111.07	3.31
15min	101.57	2.92	101.27	2.45	101.53	2.60
20min	91.60	2.36	91.53	2.19	91.53	2.10
25min	91.17	2.31	90.93	2.23	90.77	2.10
30min	92.37	2.99	92.50	2.89	92.50	2.96
40min	101.17	2.29	101.20	2.28	101.60	2.66
50min	101.17	2.29	101.23	2.40	100.87	1.91
60min	111.00	2.05	111.13	2.11	111.27	2.16
80min	111.73	2.56	111.60	2.55	111.10	2.45
100min	110.87	2.19	111.07	2.38	111.27	2.53
120min	111.87	2.67	111.53	2.57	111.23	2.46
140min	108.40	6.25	108.40	6.25	109.05	5.65
160min	109.14	4.45	112.43	3.51	114.57	3.78

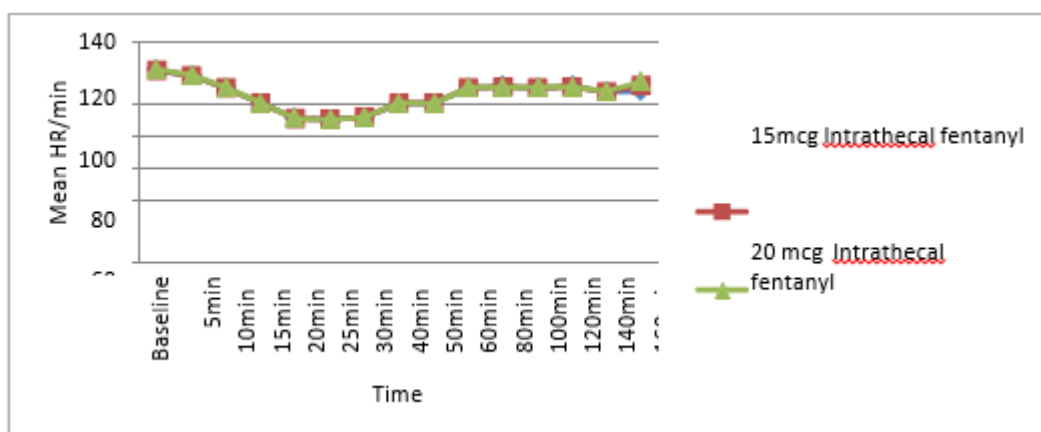


Figure 5: Line diagram showing heart rate trends among the groups

There was no significant difference among the heart rate trends among the groups ($p>0.6$). There was a decrease in heart trends 20-25min post administration of analgesia in all the groups. None of the patients developed bradycardia.

Blood pressure

Table 14: Comparison of Systolic blood pressures among the groups

SBP mm of Hg	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baseline	117.90	5.01	117.00	5.77	115.00	5.77
5min	114.70	5.19	113.40	5.68	111.40	5.68
10min	110.50	7.22	108.60	7.11	106.60	7.11
15min	104.50	5.32	102.60	5.46	100.60	5.46
20min	102.10	8.61	100.40	8.90	99.47	7.79
25min	108.10	4.91	105.30	4.59	103.20	4.05
30min	110.50	3.81	108.30	3.97	104.80	3.62
40min	111.10	5.50	109.20	5.08	106.20	4.85
50min	111.70	3.78	109.60	3.73	106.13	3.56
60min	114.60	3.79	112.70	4.22	110.00	4.61
80min	110.40	4.34	108.30	3.97	104.47	3.85
100min	111.60	5.47	109.20	5.08	106.93	4.51
120min	111.70	3.78	109.60	3.73	107.47	3.79
140min	109.50	5.80	108.40	6.25	107.25	6.27
160min	111.00	5.13	109.14	4.45	107.14	4.45

Table 15: Comparison of Diastolic blood pressures among the groups

DBP mm of	Group		
	15mcg Intrathecal	20 mcg Intrathecal	25mcg Intrathecal

Hg	fentanyl		fentanyl		fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baseline	77.33	7.51	75.80	7.90	72.87	8.32
5min	76.27	5.89	73.60	6.67	70.93	6.74
10min	72.60	7.50	70.60	7.50	68.20	7.69
15min	70.53	8.03	68.20	8.01	66.47	7.50
20min	67.70	7.83	65.30	7.53	62.57	7.29
25min	70.00	7.11	68.00	7.11	65.20	7.08
30min	71.67	6.43	69.60	6.73	67.00	6.88
40min	71.97	6.49	71.10	7.28	68.57	6.84
50min	73.27	6.05	71.80	6.40	69.33	6.35
60min	74.33	6.81	71.80	6.71	69.80	6.71
80min	71.07	5.89	69.60	6.73	67.47	6.43
100min	72.17	6.92	71.10	7.28	70.20	7.30
120min	74.07	6.53	71.80	6.40	69.87	6.28
140min	75.24	5.16	73.20	5.45	71.20	5.00
160min	76.00	2.83	75.14	2.54	72.57	2.23

Table 16: Comparison of Mean arterial pressures among the groups

MAP mm of Hg	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baseline	90.84	6.54	89.53	7.11	86.91	7.36
5min	89.09	4.94	86.87	5.57	84.42	5.60
10min	85.24	6.93	83.27	6.87	81.00	6.97
15min	81.84	6.81	79.67	6.83	77.84	6.52
20min	79.16	7.82	77.00	7.74	74.87	7.15
25min	82.69	5.86	80.43	5.78	77.87	5.57
30min	84.60	5.33	82.50	5.57	79.60	5.25
40min	85.02	5.90	83.80	6.29	81.11	5.87
50min	86.09	4.93	84.40	5.25	81.60	5.20
60min	87.77	5.40	85.43	5.55	83.20	5.45
80min	84.19	5.12	82.50	5.57	79.80	5.33
100min	85.31	6.11	83.80	6.29	82.44	6.00
120min	86.62	5.30	84.40	5.25	82.40	5.21
140min	84.90	8.21	84.93	4.21	83.22	4.06
160min	87.67	3.21	86.48	2.74	84.10	2.65

There was no significant difference among the systolic, diastolic as well as mean arterial blood pressure trends among the groups ($p>0.9$). there was a decrease in blood pressure trends 20-25min post administration of analgesia in all the groups. there was no occurrence of hypotension in any groups at any time interval the mean blood pressure remained higher in group a and lesser in group c.

Respiratory rates and Oxygen saturation of haemoglobin

Table 17: Comparison of respiratory rates between the groups

RR/min	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baseline	16.40	.97	16.47	.94	16.50	.82
5min	16.53	.78	16.50	.78	16.47	.73
10min	16.33	.76	16.33	.76	16.27	.69
15min	15.17	.38	15.17	.38	15.13	.35
20min	15.40	.50	15.43	.50	15.43	.50
25min	15.87	.78	15.93	.78	15.97	.81
30min	15.53	.86	15.47	.90	15.40	.93
40min	14.83	.38	14.83	.38	14.87	.35
50min	16.03	.67	16.10	.66	16.10	.71
60min	16.00	.00	16.00	.00	16.00	.00
80min	16.37	.96	16.37	.93	16.40	.81
100min	16.57	.77	16.60	.77	16.57	.73
120min	16.17	.91	16.20	.89	16.20	.76
140min	15.65	.59	15.65	.59	15.65	.59
160min	16.14	.69	16.43	.79	16.14	.69

Table 18: Comparison of SpO2 (oxygen saturation) between the groups

SpO2	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baseline	98.50	.51	98.53	.51	98.47	.51
5min	98.00	.00	98.00	.00	98.00	.00
10min	99.00	.00	99.00	.00	99.00	.00
15min	98.00	.00	98.00	.00	98.00	.00
20min	98.00	.00	98.00	.00	98.00	.00
25min	98.00	.00	98.00	.00	98.00	.00
30min	97.50	.51	97.47	.51	97.53	.51
40min	98.50	.51	98.47	.51	98.53	.51
50min	98.00	.00	98.00	.00	98.00	.00
60min	99.00	.00	99.00	.00	99.00	.00
80min	98.50	.51	98.53	.51	98.47	.51
100min	99.00	.00	99.00	.00	99.00	.00
120min	99.00	.00	99.00	.00	99.00	.00
140min	99.00	.00	99.00	.00	99.00	.00
160min	99.00	.00	99.00	.00	99.00	.00

There was no significant difference in mean respiratory rates between the groups at all the intervals ($p > 0.7$) There was no significant difference in mean SpO2

values between the groups at all the intervals ($p > 0.8$). There was no incidence of respiratory depression or desaturation in any of the groups

Duration of labour

Table 19: Comparison of duration of labour between the groups

Duration in min	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
I STAGE	92.67	9.54	93.67	10.25	93.33	10.61
II STAGE	28.17	5.65	27.50	5.21	27.67	5.04
III STAGE	17.17	2.52	16.83	2.45	17.00	2.49

The mean duration of First stage of labour in Groups A, B and C respectively were 92.67 $\pm$ 9.54min, 93.67 $\pm$ 10.25min and 93.33 $\pm$ 10.61 respectively. The mean duration of Second stage of labour in Groups A, B and C respectively were 28.17 $\pm$ 5.65min, 27.50 $\pm$ 5.21min and 27.67 $\pm$ 5.04 respectively. The mean duration of Third stage of labour in Groups A, B and C respectively were 17.17 $\pm$ 2.52min, 16.83 $\pm$ 2.45min and 17 $\pm$ 2.49 respectively. There was no significant difference in the duration of labour between the groups ($p > 0.8$). There was no incidence of prolongation of labour in any of the groups.

Mode of delivery: In group A, 2 out of 30 patients (6.7%) underwent Cesarean section, whereas 28 (93.3%) patients had a normal delivery. In groups B and C, all patients underwent normal delivery. There was no statistically significant difference among the groups ($p = 0.1$) Birth weight of new-born: The mean birth weights of new-born in groups A, B and C were 2.86 $\pm$ 0.38 kg, 2.82 $\pm$ 0.35 kg and 2.82 $\pm$ 0.33kg. There was no significant difference in mean birth weight between the groups ($p = 0.9$)

APGAR score

Table 20: APGAR score comparison between the groups at 1 and 5 minutes

	Group					
	15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
	Mean	SD	Mean	SD	Mean	SD
Baby Apgar_1min	8.50	0.51	8.50	0.51	8.50	0.51
Baby Apgar_5min	9.00	.00	9.00	.00	9.00	.00

There was no difference between the APGAR scores at 1 minute and 5 minutes between the groups ($p > 0.9$)

NICU Admissions

Table 21: Comparison of NICU admission rates among the groups

		Group					
		15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
		Count	%	Count	%	Count	%
NICU admission	Yes	0	0	0	0	0	0
	No	30	100.0	30	100.0	30	100.0

Among the three groups, none of the babies had NICU admissions

Side effects

Table 22: Comparison of side effects like nausea, vomiting and pruritus among the groups

		Group					
		15mcg Intrathecal fentanyl		20 mcg Intrathecal fentanyl		25mcg Intrathecal fentanyl	
		Count	%	Count	%	Count	%
Nausea	N	30	100.0%	30	100.0%	30	100.0%
Vomiting	N	30	100.0%	30	100.0%	30	100.0%
Pruritus	N	28	93.3	26	86.7	22	73.3
	Y	2	6.7	4	13.3	8	26.7

Among the three groups, none of the parturients experienced side effects such as nausea or vomiting. Among the groups, 2 parturients in group A (6.7%), 4 in group B (13.3%) and 8 in group C (26.7%) experienced pruritus, but was not statistically significant ($p=0.09$)

Discussion

A study entitled “COMPARISON OF THREE DOSES OF INTRATHECAL FENTANYL (15mcg, 20mcg and 25mcg) FOR LABOUR ANALGESIA” was undertaken in Vani Vilas hospital attached to Bangalore Medical College and Research Institute, Bangalore to compare the analgesic effect of 15mcg, 20mcg and 25mcg intrathecal fentanyl for labour analgesia and to find the effective and safe dosage of the drug for labour analgesia. To detect a minimum of 25min difference in duration of analgesia between the three groups, with alpha error of 5% and beta error of 20%, sample size calculated was 30 in each group. We have included the same.⁸

In this study, Group A received 15mcg intrathecal fentanyl, Group B received 20mcg intrathecal fentanyl and Group C received 25mcg intrathecal fentanyl. The study drug was diluted in normal saline to a total volume of 1mL in all cases. At

3-5cm of cervical dilatation as assessed by the obstetrician, after taking aseptic precautions, L3-L4 intervertebral space identified and lumbar puncture was done. After clear and free flow of CSF was seen, the study drug was injected intrathecally.

Demographic data: Demographic data comparing age, anthropometric parameters and ASA grade showed no statistically significant difference among the groups.

Hemodynamic variables

In our study, there was no significant difference in heart rates between the groups at all the intervals. There was a decrease in heart rate trends 20-25min post administration of analgesia in all the groups, but there was no occurrence of bradycardia. There was no significant difference in mean SBP between the groups at all the intervals. There was no significant difference in mean DBP between the groups at all the intervals.^{9,10} There was no significant difference in mean arterial blood pressures between the groups at all the intervals. There was no occurrence of hypotension at any of the groups at any time interval. There was no significant difference in mean SpO₂ and respiratory rates between the groups at all the intervals. There was no occurrence of desaturation or respiratory depression at any time interval in any of the groups.¹¹

Visual analogue scale scores and analgesia

Visual analogue scale was used to assess pain relief. In our study, we have used a 100mm linear visual analogue scale. Our study observed a significant difference in mean VAS Score between the groups at all the intervals except at baseline and after 100min. The mean VAS scores were higher in Group A compared to groups B and C.

Onset of analgesia: The mean durations of onset of analgesia were 13+/-1 min, 9+/-1min and 5+/-1 min in groups A, B and C respectively. Onset of analgesia was significantly faster in group C than group B and group A.

Duration of analgesia: Mean duration of analgesia in groups A, B and C respectively were 56+/-2.5min, 73.5+/- 4.4min and 89.4+/-3.2min. Group C had the longest duration of analgesia compared to groups B and A.

Need for rescue analgesia: Among the groups, 11 patients in group A, 3 in group B and none in group C required administration of rescue analgesia.

Cascio M et al studied the effects of intrathecal fentanyl on plasma catecholamine levels in term labouring parturients and concluded that there was a significant decrease in plasma epinephrine levels by 52% ($p < 0.01$), because of the decreased VAS (pain score) scores, in turn reducing the stress of labour.¹²

Clement P et al studied intrathecal narcotics for labour analgesia and found that they represent a safe and effective alternative to conventional epidural analgesia and provide significant, rapid relief of labour pain. 150 labouring parturients received intrathecal fentanyl (25mcg) and intrathecal morphine (0.25mg). The pain before and after administration was assessed by VAS scores. At 2 weeks follow up, 94% agreed that labour analgesia with intrathecal narcotics provided effective analgesia.¹³

Van Decar T et al determined the dose response relationship for intrathecal fentanyl in labouring patients and concluded that intrathecal fentanyl produces rapid, profound labour analgesia with increasing doses with no much difference after increasing the dose beyond 25 mcg intrathecally.¹⁴ Mandell GL et al studied the hemodynamic effects of subarachnoid fentanyl 25mcg in labouring parturients. They found that there was a decrease in maternal systolic, diastolic and mean arterial pressures and also the heart rates. This was attributed to the decrease in pain scores and catecholamine levels in the mother.¹⁵

The above studies correlate well with our study because our study observed a significant decrease in VAS scores post injection of intrathecal fentanyl in all the groups. But, our study observed no significant changes in hemodynamic parameters like heart rates and blood pressures. Craig M Palmer et al studied the dose response relation of intrathecal fentanyl (5-45mcg) for labour analgesia in 84 patients in active labour and concluded that intrathecal fentanyl produces rapid, profound labour. They found median effective dose of fentanyl is 14mcg. The Mean VAS scores were < 10 within 5 minutes post injection in 20-25mcg groups and within 10minutes post injection in 15mcg group. The duration of analgesia increased with increasing dose of fentanyl and ranged from 70-90min in 15-25mcg groups. Also, there was no benefit to increasing the dose beyond 25 mcg, when used as sole agent for intrathecal labour analgesia.¹

In our study, the mean VAS scores were <20 within 5 minutes post injection in 25mcg group alone. Vas scores <20 were observed in 20mcg and 15mcg intrathecal fentanyl within 10min and 15min respectively. Celeski DC et al studied the comparison of three different doses of intrathecal fentanyl for labour analgesia and found no difference in duration of analgesia between 25 mcg, 37.5 mcg and 50 mcg intrathecal fentanyl with mean duration varying from 95-105minutes ($p>0.05$).¹⁵

Conclusion

Our study comparing the analgesic effects of three doses of intrathecal fentanyl (15mcg, 20mcg and 25mcg) has yielded following results:

Good quality with faster onset and long duration of analgesia with 20mcg and 25mcg intrathecal fentanyl

No deleterious effects on new-born and labour outcomes

No side effects except pruritus which was more with 25mcg intrathecal fentanyl, but not significant statistically.

In our study, 20 mcg and 25 mcg intrathecal fentanyl proved to be effective dosage in multigravida parturients for labour analgesia compared to 15 mcg intrathecal fentanyl and 20 mcg intrathecal fentanyl was safer than 25 mcg intrathecal fentanyl due to fewer incidences of side effects like pruritus.

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