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THE ADD ON EFFECT OF FENTAYL FOR POST CEASAREAN ANALGESIA : RANDOMIZED DOUBLE BLIND STUDY

Anesthesiology

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ABSTRACT

Backfround and objective- Cesarean delivery patients require more compelling reasons to achieve optimal postoperative pain relief because they need to ambulate, to be alert and energetic enough to care for, interact with and breastfeed their new born. The aim of the study is to assess the motor and sensory results by single prick with addition of fentanyl with bupivaicane.

MATERIAL AND METHOD- With computer generated table randomly 80 parturients selected between 20 and 30 yrs undergoing elective cesarean delivery who enrolled for the study .All those with any medical/surgical complications,comorbidities,with fetal complications or high risk pregnancy,not willing to participate were excluded.Two groups were formed 1.Group B (Control group)Received intrathecally 2ml of 0.5% hyperbaric bupivacaine with 0.25ml of Normal saline.

2.Group BF (Study group) Received intrathecally 2ml of 0.5% hyperbaric bupivacaine with 0.25 ml of (12.5µg) fentanyl.

The study population evaluated under various parameters for effect of analgesia.

Result : The time taken in onset of analgesia(1.8±0.5 min VS 1.66±0.38 min, group B Vs group BF) and to achieve the highest level of analgesia (6.8±0.88 Vs 6.23±0.89,group B Vs group BF) is similar in both the group.But the two segment sensory regression was significantly high in study group(114.75±31.52 min) as compare to control group(86.63±17.11min) P<0.0001 HS. The post anesthesia complications were Nausea/vomiting and shivering .(p>0.05)

CONCLUSION: Use of intrathcal fentanyl in a dose of 12.5µg will help in producing excellent quality and prolong duration of analgesia with a single injection and with no major adverse effect on mother.

ABBREVIATION-HB-Hyperbaric bupivacaine,IB-Isobaric bupivacaine,IT-Intrathecal,IV-Intravenous,LA-Local anaesthetics,LSCS-Lower segment caesarean section, SAB-Subarachnoid block,kg-kilogram,µg –microgram,ml- mililitre,min-minute,mg-miligram.

KEYWORDS

ASA, Intrathcal Fentanyl, Hyperbaric Bupivacaine, Subarachnoid Block

BACKGROUND AND OBJECTIVE-

Today anesthesiologists' play diverse roles in modern hospitals, but the first &foremost duty of each anesthesiologist is mitigation of pain. Cesarean section is one of the most common surgeries in the world, which has been increased in the last 21 years.

The technique of subarachnoid block is simple and single injection results in ideal operating conditions and preferred means for cesarean delivery. It carries high efficiency, minimal neonatal depression, awake mother and lesser incidence of aspiration pneumonitis.The only drawback of Hyperbaric lignocaine hydrochloride is short duration and its association with transient neurological symptoms.

The purpose of this study is to compare the analgesic effect of intrathecal bupivacaine and bupivacaine with fentanyl during & after cesarean delivery.

MATERIALS AND METHODOLOGY

The Local ethical committees permission taken and a randomized placebo controlled double blind prospective study conducted at Jawaharlal Nehru Hospital and Research Centre Bhilai, Chhattisgarh, in the duration of June 2013 to April 2014. A total of 80 parturients of ASA physical status I & II aged between 20 and 30 yrs undergoing elective cesarean delivery were enrolled as per inclusion criteria.

INCLUSION CRITERIA: All elective LSCS with none of the factor in exclusion criteria.

Exclusion Criteria:-

1. In whom regional Anaesthesia is contraindicated
2. Complicated Pregnancies such as- multiple pregnancies, Placenta Previa, pregnancy induced hypertension.
3. Antenatal Patients with acute fetal distress & fetal abnormalities.
4. Pregnancy with medical illness (cardiovascular, respiratory, renal, endocrine)
5. Inability to understand the visual analogue scale.
6. Patients not willing to participate in the study.
7. Patients with allergy to study medications.

METHOD

- A thorough preanaesthetic check up was done before the surgery with all routine investigations. All the patients were informed regarding the procedure and a written consent was obtained from all the patients.
- Age, Height, Weight, Pulse Rate, Blood Pressure and Respiratory rate were recorded. Visual analogue scale was explained to the patients. Usual overnight fasting regime was followed for the all cases.

Total 80 patients were randomly allocated into 2 equal groups of 40 each with the help of computer generated table of random numbers.

Group B (Control group): Received intrathecally 2ml of 0.5% hyperbaric bupivacaine with 0.25ml of Normal saline.

Group BF (Study group)

Received intrathecally 2ml of 0.5% hyperbaric bupivacaine with 0.25 ml of (12.5µg) fentanyl.

The study was kept double blind by:

1. Patient was not told about the content of the drug which she receives intrathecally. The spinal drug was prepared by an anesthesiologist not involved with data collection.

TECHNIQUE

On operating table, before procedure monitors (NIBP cuff, pulse oximeter, ECG) were attached and baseline value of BP, HR, SpO_2 and RR were recorded. A 16 G IV Cannula was inserted. All patients received preloading with 15-20 ml/kg of Ringer lactate solution followed by infusion at the rate of 10-15ml/kg/hrs. Other fluids and blood were given as indicated.Fetal heart rate was noted. Lumbar puncture was carried out using 25G Quincke spinal needle in sitting position at L_3-L_4 Interspace and the drug prepared as per group of patients was injected with a uniform speed.After noting the time of injection patient was immediately placed in supine thereafter with left uterine displacement. All patients received supplemented oxygen. Sensory level was tested by pinprick at the left midclavicular line Time of onset of sensory block Motor block grade III motor block was recorded. During intraoperative period pulse rate, blood pressure,respiratory rate and oxygen saturation were recorded every 2 min for first 10 min and then every 15 min up to one hour and every 30 min thereafter upto 270 minutes (2, 4, 6, 8, 10, 15, 30, 45, 60, 90, 120, 150, 180, 210, 240, 270).

Postoperatively

The patients were monitored in the post-anaesthesia care unit. Time taken for recovery of sensory level to two dermatomal segments below the highest level was noted. Postoperatively the patients were evaluated for pain at the operation site with visual analogue scale 0 to 10(0 = No pain, 10 = Worst pain). Time interval between injection of spinal drug to first reports of pain was noted i.e. considered as the duration of sensory analgesia. Systemic narcotic analgesics were not given until VAS was more than 4.Time taken from the administration of subarachnoid block to the patient's first on demand analgesic drug for pain was noted i.e. considered as the duration of effective analgesia.

Recording of parameters

Following parameters were noted.

1. Time of injection of drug.
2. Time of onset of sensory block
3. Maximum level of sensory blockade achieved.
4. Time of onset of motor block
5. Quality of motor block
6. Time from injection to delivery of newborn interval.
7. Time for two segment regression.
8. Time taken for regression of sensory block by two dermatome below the heighest sensory level.

9. Duration of analgesia

a) Duration of complete analgesia
b) Duration of effective analgesia which was defined as –
10. Time from subarchoid injection to first dose of rescue analgesic.(VAS score>4).
11. Duration of motor block
12. Apgar score of the newnorn at 1 minute and 5 minutes.

The all collected data enter into excel sheet and calculated by SPSS 11.5 system for statistical analysis. Univariate and bivariate analysis were carried out using the Student *t* test for the continuous variable (age) and two-tailed Fisher exact test or chi-square (^{2}) test for categorical variables.

RESULTS

The mean age of the study population was 24.85 ±1.9 year in group B and 25.15 ±2.29 year in group BF with no statistical difference in age group of either group.(Table 1)

The Onset of sensory analgesia assessed at T10 level and 62.5% participants in Group B had onset time of 2-3 min as compare to group BF with 100% in 1-2 min. Though difference in the mean time between Group B and Group BF was not statistically significant t= 1.41 (p › 0.05).(Table 2)

The time taken to achieve highest level of analgesia in Group B was 7-8 mimute (mean 6.8 ±0.88 minutes) in 55 % as compare to group BF ,where 5-6 miutes (mean 6.23 ± 0.89 minutes,) were taken in maximum number(72.5%) of cases (p>0.05) (Table 3)

The segments of various dermatome was assessed and it was equal in both the group with maximum effect on T_4 level.(Table 4)

The difference in the mean time taken for two segment sensory regression between Group B (Mean±SD 86.63±17.11 minute)and Group BF (Mean±SD 114.75±31.52 minute) was statistically significant (p < 0.05).(Table 5) but for motor block the onset and duration was similar in both the groups (p>0.05).(Table 6 & 7)

The significant post anesthesia complications were Nausea/vomiting and shivering in Group B,seen in 25% , 20% respectively as compare to Group BF (p<0.05).(Table 8)

TABLE-1

Mean age (years)

Groups	Mean±SD (Age in years)	Unpaired 't' value	Significance
Group B	24.85 ±1.9	0.52	P>0.05
Group BF	25.15 ±2.29		

*DF=78

T=0.0.52 ;p>0.05, not significant

TABLE-2

Time of onset of sensory analgesia

Time of onset of Analgesia at T10 (Min)	Group B		Group BF	
	No of Patients	Percentage	No of Patients	Percentage
1-2	15	37.5	40	100
2-3	25	62.5	0	0
3-4	0	0	0	0
Total	40	100	40	100
Mean±SD (Time in min.)	1.8±0.5		1.66±0.38	P>0.05

Unpaired 't' value= 1.41

TABLE-3 Time Taken to achieve highest level of sensory analgesia (min)

Time Taken to achieve highest level of sensory analgesia (min)	Group B		Group BF	
	No of Patients	Percentage	No of Patients	Percentage
1—2	0	0	0	0
3—4	0	0	0	0
5—6	18	45	29	72.5
7—8	22	55	11	27.5
9—10	0	0	0	0
Total	40	100	40	100
Mean±SD (Time in min.)	6.8±0.88		6.23±0.89	P>0.005 NS

Unpaired 't' value 2.88

TABLE -4 Maximal dermatomal level achieved

Dermatomal Level	Group B	Group BF
T3	4	8
T4	23	28
T5	0	3
T6	13	1

TABLE-5 Time for two segment sensory regression

Time for two segment regression(min)	Group B		Group BF	
	No of Patients	Percentage	No of Patients	Percentage
60-79	7	17.5		
80-99	25	62.5	15	37.5
100-119	5	12.5	12	30
120-139	2	5	1	2.5
140-159	1	2.5	6	15
160-179	0	0	5	12.5
180-199	0	0	1	3
200-219	0	0	0	0
Total	40	100	40	100
Mean±SD (Time in min.)	86.63±17.11		114.75±31.52	P<0.0001 HS

Unpaired 't' value 4.958

TABLE 6 Time of onset of Grade III motor block

Time of onset of grade III motor block (min)	Group B		Group BF	
	No of Patients	Percentage	No of Patients	Percentage
1—2	8	20	29	72.5
3—4	31	77.5	10	25
5—6	1	2.5	1	2.5
Total	40	100	40	100
Mean±SD (Time in min.)	3.10±0.74		2.33±0.62	p>0.05.

Unpaired 't' value t=1.6

TABLE 7 Total duration of Grade III motor block

Total Duration of grade III motor block (min)	Group B		Group BF	
	No of Patients	Percentage	No of Patients	Percentage
90-119	23	57.5	17	42.5
120-149	16	40	10	25
150-179	1	2.5	6	15
180-209	0	0	7	17.5
Total	40	100	40	100
Mean±SD (Time in min.)	109.88±17.81		130.38±37.9	p>0.05

Unpaired 't' value 3.09

TABLE 8 Complications during anaesthesia

Complication	Group 1		Group 2		P value	Inference
	N	%	N	%		
Hypotension	16	40	16	40	P>0.05	NS
Bradycardia	5	12.5	4	10	P>0.05	NS
Nausea and Vomiting	10	25	3	7.5	P<0.05	S
Respiratory Depression		0		0		
Shivering	8	20	2	5	P<0.05	S
Pruritus	0	0	3	8	P>0.05	NS
Post dural puncture headache and Neurological Complication	-					
Foetal bradycardia	-					

DISCUSSION

August Bier in (1898) produced true spinal anaesthesia in animals and man. Actually introduced the techniques as an anaesthetic mode.

Subarachnoid block is commonly used method of regional anaesthesia for cesarean section because of its ease,reliability,and cost effectiveness.

The use of neuraxial opioids have increased as they improve the quality of intraoperative analgesia produced by local anaesthetics, by binding directly with spinal opiate receptors and prolong the duration of postoperative analgesia.

Malinovsky JM et al (1991) in a study concluded that intrathecal use of midazolam should be avoided in humans.**Gielen M.J. M, et al in (1993)** reported that fentanyl is one of the safest opioids. **Gissen A.S, et al in 1987** have demonstrated the safety of fentanyl regarding neurotoxicity.

Fentanyl citrate is a synthetic opioid analgesic has a rapid onset and a shorter duration of action (dose dependent) following intrathecal administration. With local anaesthetic, many of its clinical actions can occur during intraoperative period. It is a safer than morphine for management of early post operative pain as it does cause delayed respiratory depression when administered intrathecally.

Siddik – Sayyid et al (2002) compare the same dose of fentanyl intrathecally Vs intravenously during cesarean delivery and found that the synergistic effect of fentanyl on bupivacaine was able to reduce the dose of bupivacaine and decrease intraoperative analgesic requirement & side effects.

In a preliminary review of literature we found that a does of 6.25-25 µg would be optimum for our purpose without significant side effects on the mother and neonate.

Since both the groups were demographically similar (p>.05 in all comparisons) it can be presumed that the groups were comparable for the purpose of the study.

No premedication was used in the study population, it can therefore be presumed that recording of parameters pertaining to sensory analgesia were consistently accurate. All the parturients were preloaded to offset the effect of relative hypovolaemia on hypotension.

Characteristics of sensory blockade

Time of onset of sensory block

Sergio D. Belzarena(1992) assessed effects of intrathecally administered fentanyl.Level of analgesia to pinprick and time to achieve them were similar in the groups. **Catherine O' Hunt et al.(1989)**studied the duration of analgesia for various intrathecal fentanyl dosage with bupivacaine .They did not comment on the time of onset of sensory analgesia at T_{10}.The present study included this period and defined the onset for both sensory and motor blocks.

Dr. B.N. Biswas et al (2002) used 12.5 µg of intrathecal fentanyl with 10 mg. of hyperbaric bupivacaine and concluded that the onset of bupivacaine induced spinal block was not enhanced in fentanyl group. The time of onset of sensory block was taken as the time taken from administration of the drug intrathecally to the loss of pinprick sensation at T_{10} dermatome level bilaterally in the present study.

Time taken to achieve highest level of sensory analgesia

The Highest level of analgesia was found at T_4 level in the present study, with mean time in Group B was 6.8±0.88 minutes and in Group BF was 6.23 ±0.89 minutes ($p < 0.05$) similar to **Shende D *et al*** (6.5 Vs 8 min) and **B N Biswas et al. (2002)**[10]study(8 ± 2.1minutes Vs 7 ± 2.4minutes) with no stastical significance.

Time for two segment regression of sensory block

Time for two segment regression was taken as the time taken for regression of two dermatome segments below the highest sensory level.

In the present study, maximum time taken was 140 minutes and the minimum time taken was 50 minutes and mean time was 86.63±17.11 minutes in Group B.

In Group BF maximum time taken was 190 minutes and minimum time taken was 80 min and the mean time was 114.75±31.5 minutes. The difference in the mean time between Group B and Group BF was statistically significant ($p < 0.05$). Thus in our study time for two segment regression was significantly prolonged with the addition of fentanyl to bupivacaine.

According to **Harbhej Singh et al. (1995)** the time taken for two segment regression was prolonged in fentanyl with bupivacaine group. In Group I was 74 ± 18 minutes and in Group II(with fentanyl)it was 93 ± 22 minutes, it was statistically significant.. Similar results were noticed with **Uma Srivastava et al. (2004**) and **Benhamou Dan et al.(1998)** studies.

Dr. B.N. Biswas et al(2002)[10], found that time to two segment regression was significantly longer when 12.5 µg fentanyl added to 10mg of hyperbaric bupivacaine

P.R.Dhumal (2013)observed that opioids have synergistic effect with local anaesthestics and mean time for two segment regression and complete sensory recovery was significantly prolonged in group with fentanyl.

Our results concurs with findings of the above authors.

Duration of analgesia

Duration of complete analgesia

In the present study, duration for complete analgesia was defined as the time from subarchoid injection to first report of pain (VAS >0).

The maximum duration for complete analgesia in Group B was 250 minutes and the minimum was 80 minutes and mean duration was 176.25±28.03 minutes. In Group BF maximum time for complete sensory recovery was 330 minutes and minimum time was 170 minutes and the mean time was 260.13±33.71 minutes.The difference in mean time between Group B and Group BF was statistically significant ($p < 0.05$). The time for complete sensory recovery was prolonged in Group BF when compared to Group B. Our results in the present study concurs with previous studies.[8,10,12]

Duration of effective analgesia

The total duration of effective analgesia was taken as the time interval between the injection of the spinal drug to first dose of rescue analgesics.

Catherine O'Hunt et al. (1989),[9] in their study elaborated the duration of effective analgesia with fentanyl 6.25 µg.Further various studies like **Gunnan Dahlgren et al (1997)**,**B N Biswas et al. (2002)**[10] **Sahar M. Siddik et al (2002**)[7] came with different doses and reflected their results with prolong analgesia.we also found our results similar to previous studies.

Motor blockade characteristics

The significant result is the duration of motor blockade is similar in either group. Thus the addition of fentanyl to bupivacaine did not affect the onset of motor block. Similar results were noticed in the studies conducted by previous authors who found that onset and extent of motor block did not differed irrespective of increased concentration of intrathecal fentanyl 6.25, 12.5, 25, 37.5 and 50 µg.[9,10,12,] which give conclusion of choice of dose of fentanyl as per need of analgesia in post operative period. In our study we have taken a minimum dose by choice of 12.5 µg for proper follow up and need of analgesia timing assessment.

It is also seen in previous studies that the motor recovery timing did not change by addition of fentanyl.[10,]

Complications :

Nausea & Vomiting was very frequent complication but found significantly lower in group BF. t= 2.18 P<0.05.This finding is in corroboration with those of Palmer CM et al. (1995) Gunnan Dahlgren et al (1997)[16] Theodore R. Moullaong et al (2002) .Thus the fentanyl gave added advantage of antiemetics over analgesia in the study population. Chow TC et al (1994) who in their study concluded that low dose intrathecal fentanyl 12.5 µgm is a good method for decreasing both incidence & severity of shivering during spinal anaesthesia.This was seen in our study as well and also justifies the choice of dose for the study.

The pruritus was seen in 8% cases which was noticed in high doses with other studies.Thus the choice of 12.5 µg results with lesser side effects.[7,9]

None of the patients in this study experienced any neurological complication during postoperative follow-up.

Previous studies also reflected with respiratory depression in first 24 hours,though the doses were different in all studies, which was not seen in our study.[8,12,]

CONCLUSION

- From the present study it is concluded that,Intrathecal fentanyl as an adjuvant to intrathecal hyperbaric bupivacaine (0.5%) in a dose of 12.5µg-
- Provides significant prolongation of duration of sensory block and effective analgesia.
- No significant difference in onset and duration of motor block.
- Significantly decreases incidence of emetic episodes and shivering.
- Hemodynamically stable.
- Appears with minimum acceptable side effects.
- Hence we recommend the use of fentayl for its add on effects in caesarean section.

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