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Epidural Infusion of Inj. Bupivacaine Hydrochloride 0.125% Vs. Bupivacaine Hydrochloride 0.125% With Fentanyl Citrate for Post-Operative Analgesia Following Abdominal Surgery.

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ABSTRACT

We compared the postoperative epidural analgesia provided by the continuous epidural infusion of Bupivacaine hydrochloride with that provided By a continuous infusion of bupivacaine hydrochloride plus fentanyl citrate.100 patients were randomly allocated in 2 groups of n=50 each to receive drugs .Group 1: inj. Bupivacaine hydrochloride 0.125% Group 2: inj. Bupivacaine hydrochloride 0.125% and inj. Fentanyl citrate 2mcg/ml. Vitals,Visual analogue score, Sedation score and any side effects were observed. Adding fentanyl citrate 2 mcg/ml to bupivacaine hydrochloride 0.125% significantly reduced pain and increased quality of analgesia.Observation of side effects reflects that o.125% bupivacaine hydrochloride in group 1 has significant propensity to cause nausea and vomiting.Addition of inj. Fentanyl citrate 2mcg/ml to inj. Bupivacaine hydrochloride 0.125%for continuous epidural infusion significantly improved quality of analgesia, provided uniform stable analgesia without an attendant increase in side effects.

KEYWORDS : - postoperative analgesia, epidural infusion, fentanyl citrate, bupivacaine hydrochloride.

INTRODUCTION

The International Association for the Study of Pain (IASP) has defined pain as "an unpleasant sensory & emotional experience associated with actual or potential tissue damage or described in term of such damage."[1] Post-operative pain, especially when poorly controlled, results in harmful acute effects (adverse physiological responses) and chronic effects (delayed long term recovery and chronic pain).

Continuous infusion epidural analgesia (CIEA) technique focus on the relative high total bupivacaine hydrochloride dosage. One of the important developments in the past decade has been the epidural administration of an opioid, alone or in combination with a local anaesthetic.

Local anaesthetic administration by the epidural route is one of the most effective pain relieving treatment modality. However local anaesthetic drugs in higher concentrations can cause undesirable side effects like hypotension, bradycardia and loss of motor power.[6] Hence opioids may be added to improve post-operative analgesia. Due to their synergistic action at the dorsal horn a small dose of opioid combined with local anaesthetic potentiates analgesia.

METHODS

This study was conducted at Gujarat Cancer and Research Institute during the year 2011-2013 with the permission of ethical committee of hospital and after the informed consent of 100 adult patients of ASA grade 1&2. Patients with history of drug allergy, regular consumption of analgesic or drug abuse& dependence on narcotic, valvular heart disease/congenital heart disease/arrhythmia/conduction block, COPD/liver disease, any contraindication to epidural puncture and pregnancy were excluded from study.

All patients received tablet lorazepam 1 mg at 10:00pm on the day before surgery as a premedication. 18 G epidural catheter was inserted in L2-L3 or L3-L4 vertebral space with 18 G touhy needle by hanging drop technique. Test dose of inj. bupivacaine hydrochloride 3ml 2%with 1:2,00,000 adrenaline given through epidural catheter. For intra-operative analgesia and anaesthesia purpose inj.bupivacaine 0.5% 10 cc given after general anaesthesia was administrated. After completion of surgery patient was transferred to post- operative ward for next 24 hrs. Patient's vitals i.e. pulse, blood pressure, respiratory rate, temperature and pain score were observed. Any other form of analgesia was omitted. Patients were assessed for pain score on VAS (0=no pain and 10=worst pain ever) and as they complained of pain for 1st time (t=0 min) bolus injection of 5 ml 0.125% epidural bupivacaine hydrochloride was given. Patients were then randomly allocated to study groups. Patients in group 1(n=50) and in group 2 were given a continuous epidural infusion of inj. bupivacaine hydrochloride 0.125% and bupivacaine hydrochloride 0.125% with fentanyl citrate 2 mcg/ml respectively at the rate of 5ml/hr. If this did not result in adequate pain relief, the rate of infusion was increase by 1 ml/hr. and a bolus of 5 ml of solution was administered maximum up to 3 mg/kg/hr. & 400mg/24 hrs or fentanyl citrate 1 mcg/kg/hr..

If still patient complained of pain, other analgesics like inj. Fentanyl citrate 1-2 mcg/kg intravenously given as rescue analgesic and patient was excluded from study.

All parameters and side effects were noted at t=0 min, 30 min, 1hr., 2hr., 4 hr., 8 hr., 12 hr., 16 hr., 20 hr. and 24 hr.

STATISTICAL ANALYSIS *AND RESULTS*

Statistical analysis was performed using the statistical software package. Data comparisons were made using unpaired students t-test and fisher exact test for ordinal data.

Table 1 and figure 1 shows that there were no difference in the age, weight, height and sex, in both groups & both groups are comparable using unpaired student T- test. (P> 0.05) Table 2 shows that total numbers and types of abdominal surgeries in both groups are comparable.

Pain assessment by VAS score suggests that there was no significant difference in the VAS score before starting infusion (at t=0 min group1 VAS=8.1+0.3 &group 2 VAS =8.2+0.4) (p>0.05). After starting the infusion pain relief was there in both the groups but after 30 min it was observed that VAS score was significantly low in group 2 compared to group 1 suggesting that the adding fentanyl citrate 2 mcg/ml to bupivacaine hydrochloride 0.125% significantly reduced pain and increase quality of analgesia..

Table 4 and figure 3 shows that pulse rate at starting of infusion (t=0 min) among both groups were comparable (P>0.05). After starting infusion, there was fall in pulse rate in both groups but the difference between both groups was not significant. (p>0.05) In post-operative period both group of patient showed comparable blood pressure except in first post-operative hour, 3 patients in group 1 had low blood pressure. Statistical analysis shows that there was fall in blood pressure in both groups after starting epidural infusion but the difference between both groups was not significant. (P>0.05) Statistical analysis of post-operative respiratory rate between two groups revealed no significant difference. (p>0.0.5) Observation of side effects reflects that 0.125% bupivacaine hydrochloride in group 1 has significant propensity to cause nausea and vomiting. Hypotension is observed in 46% in group 1 while in 40% in group 2. 4 patients in group 1 and 2 patients in group 2 received treatment for hypotension in the form of crystalloid infusion. Bradycardia and pruritus are comparable in both groups while sedation is observed in one patient in group 2 but not

in group 1.

DISCUSSION

Susan m Nimmo et al emphasised the proven benefit of epidural analgesia. It can be provided safely in appropriate patient undergoing major abdominal surgery. [21]

Continuous infusion not only produces a constant block to maintain analgesia, it also reduces the medical and nursing workload. R Virmani et al stated continuous infusion of bupivacaine hydrochloride provided better analgesia at rest and on movement than intermittent boluses, and is not associated with fluctuation in the level of analgesia.[11] Limy et al stated maintenance of labour analgesia using automated intermittent bolus at a bolus volume of 2.5 ml every 15 min does not decrease the incidence of breakthrough pain or analgesic efficacy compared to continuous epidural infusion.[22]

Bupivacaine are absorbed into the systemic circulation at a slower rate, resulting in longer duration of action compare to other local anaesthetic agent. The additional of bupivacaine 0.1% did not improve analgesia with epidural fentanyl citrate in patients who had undergone abdominal and thoracic surgery[23]. The addition of higher bupivacaine concentration of 0.2-0.25% or 0.5%has improved postoperative analgesia following abdominal surgery but there was higher incidence of sensory blockade and motor blockade which is not optimal for early ambulation[24]. There for 0.125% bupivacaine was found to be a more effective concentration.

Fentanyl citrate is having high lipid solubility and has rapid onset and short duration of action; low risk for delayed respiratory depression because of rapid redistribution as compared to other lipophilic opioids. Epidural dose of fentanyl is selected as 2 mcg/ml because higher dose of fentanyl citrate may have greater adverse effect than beneficial effect. [25]

Theoretically, the two drugs bupivacaine and fentanyl act by different mechanisms. Bupivacaine hydrochloride act on voltage gated sodium channel of spinal nerve root and fentanyl citrate on mu receptors of dorsal horn of spinal cord. That's why fentanyl citrate is combined with epidural bupivacaine hydrochloride. Cooper et al (1992) stated that adding fentanyl citrate to bupivacaine hydrochloride reduced the dose of bupivacaine hydrochloride by up to 68%, improves analgesia at rest and decreases PCEA use. [14]

Jaishri Bogra et al (2008) stated that 100 mcg fentanyl citrate when added to epidural 0.25% bupivacaine hydrochloride produce excellent pain relief in abdominal surgery patients with added advantage of early onset. [12] Thomas H et al (1996) proposed that there were 40%more pain free patients in bupivacaine hydrochloride-fentanyl citrate group during uterine exentration and wound closure procedure. [15]

Hypotension was mostly seen after about 4 hrs. of starting infusion which required to stop infusion for some time and easily managed by crystalloid fluid loading. Using a dose of 1mcg/kg/hr. of epidural fentanyl citrate Renaud et al observed a significant decrease in the ventilatory response to co_2 after several hours of infusion but without a decrease in respiratory rate. [26]

1 patient in group 2 had sedation which was less than grade 2(drowsy but easily aroused)and 1 patient had pruritus also. Inj. Bupivacaine hydrochloride in group 1 had greater propensity to cause nausea and vomiting (nausea 12%& vomiting 12 % in group 1 vs. nausea 6%&vomiting 6%in group 2). Dan j et al stated nausea (26.2%) & hypotension (44.6%) were most common side effects and all side effects were evenly spread across the group. [27]D.W.cooper et al (1996) incidence of nausea was 11% & vomiting was 6% in bupivacaine hydrochloride group. [14]J.D.lirzin et al (1998) incidence of nausea & vomiting 11% in bupivacaine hydrochloride (0.25%) group while 6% in bupivacaine hydrochloride &fentanyl citrate group. [28]

In conclusion, Addition of inj. fentanyl citrate 2mcg/ml to inj. bupivacaine hydrochloride0.125%for continuous epidural infusion mode of administration significantly improved quality of analgesia, provided uniform stable analgesia without an attendant increase in side effects in routine clinical setting and is therefore to be recommended.

TABLE-1
Demographic data: Values are mean ± SD

GROUP		
	Group 1	Group 2
N	50	50
Age(years)	56±10	58±9
Height (cm)	158±7	160±5
Weight (Kg)	48±8	51±3
Sex (male/female)	19:31	18:32

TABLE- 2
Comparison of surgery performed in both the groups:

Groups			
Diagnosis	Surgery	Group 1	Group 2
Ca. ovary	TAH+BSO	20	22
Ca. cervix	Wertheim's hysterectomy	6	4
Ca. stomach	Total gastrectomy	4	6
Ca. colon	Colectomy	8	8
Obstructive jaundice	Whipple's procedure	8	6
Obstructive jaundice	Triple bypass	4	4
		50	50

TABLE-3
Post-operative VAS score (mean ± SD)

Groups			
Time	Group 1	Group 2	P value
t = 0	8.1±0.3	8.2v±.4	0.2030
30 min	4.2±0.7	1.7±0.2	0.0001
1 hour	5.0±1.0	2.9±0.6	0.0001
2 hour	3.1±0.8	2.4±0.2	0.0001
4 hour	4.0±1.2	3.0±0.8	0.0001
8 hour	4.2±0.3	2.8±0.4	0.0001
12 hour	3.8±0.8	2.2±0.4	0.0001
16 hour	3.0±0.4	2.0±0.6	0.0001
20 hour	3.0±0.6	1.8±0.7	0.0001
24 hour	2.8±0.7	1.6±0.5	0.0001

TABLE-4
Changes in vital parameters (mean ± SD)

Pulse rate (beats/min)										
Time	T=0	30 min	1 hr.	2 hrs.	4 hrs.	8 hrs.	12 hrs.	16 hrs.	20 hrs.	24 hrs.
Group 1	87±9	86±9	83±8	84±10	80±8	78±9	76±10	76±7	73±2	70±7
Group 2	87±12	84±7	83±7	82±6	78±5	74±7	73±7	73±6	71±6	69±6
P value	1.00	0.24	0.85	0.16	0.17	0.04	0.16	1.00	0.12	0.53
Mean blood pressure (mm Hg)										
Time	T=0	30 min	1 hr.	2 hrs.	4 hrs.	8 hrs.	12 hrs.	16 hrs.	20 hrs.	24 hrs.
Group 1	90±10	86±9	78±8	77±2	77±7	75±6	72±7	71±6	72±5	72±5
Group 2	92±8	85±7	75±10	75±8	74±8	74±2	77±6	69±8	72±9	75±6
P value	0.12	0.08	0.10	0.12	0.33	0.08	0.18	0.10	0.07	0.37
Respiratory rate (/min)										
Time	T=0	30 min	1 hr.	2 hrs.	4 hrs.	8 hrs.	12 hrs.	16 hrs.	20 hrs.	24 hrs.
Group 1	15.4±1.4	15.5±2.2	15.2±2.7	14.7±2.2	14.8±1.1	15.5±0.9	15.0±0.7	14.6±1.2	14.1±0.9	15.0±1.8
Group 2	15.2±1.3	15.2±1.4	15.0±1.3	14.1±1.3	14.4±1.0	15.0±1.2	14.9±0.6	14.1±1.4	13.8±1.2	14.6±2.1
P value	0.46	0.41	0.63	0.10	0.06	0.16	0.44	0.05	0.16	0.30

TABLE-5
Side effects:

Group		
Side effect	Group 1	Group 2
Hypotension	23 (46%)	20(40%)
Bradycardia	2 (4%)	3(6%)
Sedation	Nil	1 (2%)
Nausea	6(12%)	3(6%)
Vomiting	6(12%)	3(6%)
Pruritus	Nil	1(2%)

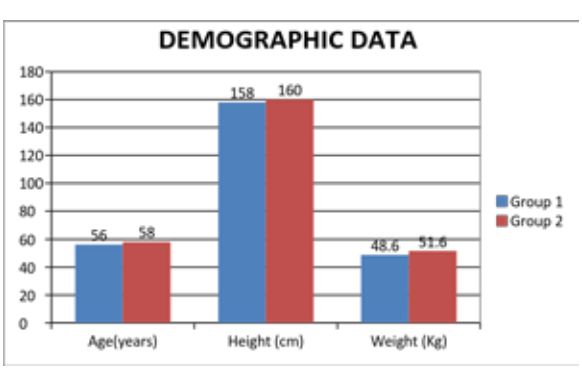

FIGURE-1

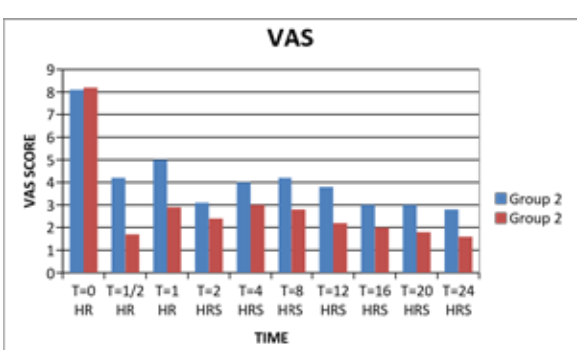

FIGURE-2

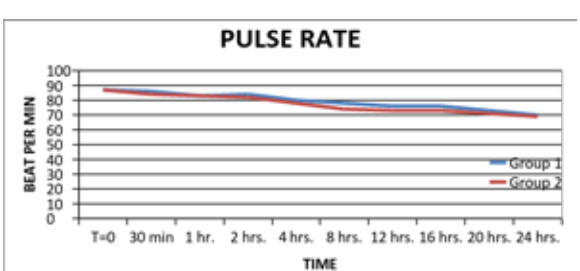

FIGURE-3(a)

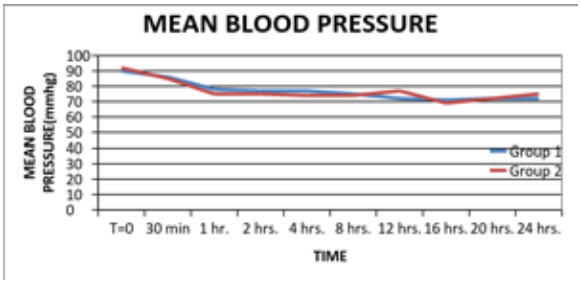

FIGURE-3(b)

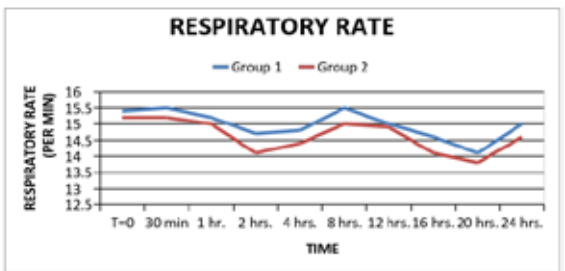

FIGURE-3(c)

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