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Comparison of epidural morphine sulphate versus epidural morphine sulphate with bupivacaine hydrochloride for postoperative pain relief in patients undergoing lower abdominal surgery

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Abstract

Background: Post-operative pain is currently a significant and common problem. It is associated with a postoperative complication, which lead to delayed recovery and prolonged hospitalization. Epidural anesthesia provides not only good postoperative analgesia but also has good hemodynamic effects.

Aim: To compare the safety and efficacy of postoperative analgesia with epidural morphine sulphate (2 mg) alone and epidural morphine sulphate(2mg) plus bupivacaine

hydrochloride 2ml (0.5%)10mg for lower abdominal surgery.

Material and method: Patients were randomly divided into two groups of 50 each posted for lower abdominal surgeries. Epidural catheter was inserted for postoperative analgesia. Group M received morphine sulphate 2mg in 10ml Normal saline and group BM received Bupivacaine hydrochloride 2ml (0.5%)10mg and Morphine sulphate 2mgdiluted in Normal saline up to 10ml. The intensity of pain and pain relief was assessed using VAS at 5, 10,15,30,60 minutes 2hours, and thereafter 2 hourly for24 hours postoperatively.

Results: Study shows that quality of analgesia in Group BM 28% patients graded pain relief as excellent with Mean±SD of 3.18±0.59, in Group M 16% patients graded their pain relief as excellent with Mean±SD of 2.88±0.71. This difference was statistically significant p=0.0237 t =2.29.

Conclusion: It can be concluded from the study that Epidural Morphine sulphate along with Bupivacaine hydrochloride is safe, effective, and reliable method of postoperative pain relief with lesser side effects and greater patient satisfaction compared to epidural morphine alone.

Keywords: Epidural anesthesia, Lower abdominal surgery, Morphine sulphate, Bupivacaine hydrochloride, post-operative pain

Introduction

Post-operative pain is currently a significant and common problem and if left untreated severe pain causes stimulation of sympathetic component of the autonomic nervous system resulting in increased release of catecholamines so increased HR, blood pressure has many negative effects including postoperative ileus and cardiac ischemia in susceptible individuals.[1] Inadequately controlled postoperative pain may immobilize the patients that ultimately prolongs the duration of hospital stay and increase the cost[2] so management of pian is one of the most challenging and gratifying domains of anesthesia[3]

The epidural route is more popular for postoperative pain management as the technique can be used alone or in combination with general anesthesia.

It has been seen that patients given epidural analgesia have significantly higher arterial oxygen tension during first three post-operative days with a lower incidence of pulmonary complication and chest infection.[4]

Epidural administration of low dose local anesthetic agents in combination with opioids has been shown to produce a greater and longer lasting antinociceptive effect. It has been proposed that opioids may bind better to spinal opioid receptor in the presence of local anesthetic.[5]

Morphine has good analgesic property comparable to others. It phenanthrene alkaloid of opium found naturally from plants and animals directly act on central nervous system and u agonist that act by decreasing voltage gated calcium channels or by opening of the inward flowing potassium channels. These effects decrease neuronal activity. [6,7] Bupivacaine a local anesthetic act by blocking inhiation and conduction of pain signal. Its analgesic property, onset and duration of action depend upon dose and concentration of drug administered.[8]

The present study was conducted to assess the safety and efficacy of postoperative analgesia with epidural morphine sulphate (2 mg) alone with epidural morphine sulphate(2mg) plus bupivacaine hydrochloride 2ml (0.5%)10mg for lower abdominal surgery. Both animal and human studies have documented synergistic effect of

epidural bupivacaine and morphine combination therapy.[9]

Merits and demerits of neuraxial opioids (13)

Merits	Demerits
Faster onset of surgical block than LA alone	Pruritis
Greater spinal anesthesia success rate	Sedation
Improved intraoperative analgesia	Respiratory depression
Permits lower dose of LA	Urinary retention, dysphoria
Postoperative analgesia beyond the duration of LA motor block	Nausea, vomiting

Aims and objective

A comparison of epidural morphine sulphate versus epidural morphine sulphate with Bupivacaine hydrochloride for postoperative analgesia in lower abdominal surgery focusing on

- Onset of analgesia.
- Duration of analgesia
- Quality of analgesia
- Cardio respiratory effects like change in pulse rate, blood pressure and respiratory rate.
- Adverse effects.

Method and material

100 adult patients of ASA grade I and II, of either sex, belonging to 25-65 years of age, posted for elective lower abdominal surgeries in general surgery and gynecology were selected for the study. Lower abdominal surgery is defined as the incision below the umbilicus and different surgeons performed the surgery. Patients were randomly divided into two groups of 50 each, all received drugs by epidural route.

Group M- Inj. Morphine sulphate 2mg in 10ml Normal saline. Total Volume=10ml

Group BM- Inj. Bupivacaine hydrochloride 2ml (0.5%)10mg and Inj. Morphine sulphate 2mg diluted in Normal Saline up to 10ml. Total Volume=10ml

Patients were visited on the previous day of the surgery, a detailed clinical history was taken, and general and systemic examinations were done.

The patients were explained about the epidural technique with catheter in situ, its advantages and disadvantages. They were also educated about the usage of Visual Analog Scale (VAS) for assessment of the intensity of postoperative pain and were instructed to mark on the scale at the point which he/she felt was representative of their level of discomfort.

A written informed consent was taken from each patient. Basic laboratory investigations like complete blood count, hemoglobin, bleeding time, clotting time, blood sugar, blood urea, serum creatinine, urine analysis, ECG and chest x-ray were carried out routinely on all patients. To allay the anxiety and apprehension, all patients were premeditated with Tablet lorazepam (0.5 mg or 1 mg) at 10 pm in the night before the surgery. Patients were kept nil per orally for 8 hrs before surgery.

Epidural catheter was inserted for postoperative analgesia and all patients were operated under General Anesthesia. The patient was made to lie supine on the operation table. An intravenous line was secured with 18G cannula and Inj Ringer lactate (R.L.) 500 ml infusion was started. Routine monitors like ECG, NIBP, Pulse oximetry was connected for all case and basal vital signs were recorded before starting the procedure. Drugs and equipment's necessary for resuscitation and general anesthesia administration were kept ready. An autoclaved epidural tray was used. Sterile disposable epidural set was used

and checked for any manufacturing problems and check that catheter can pass through needle. The patient was placed in sitting or lateral position. Under all aseptic and antiseptic precautions, a skin wheal was raised at L2- L3 interspace with of 2% Lignocaine. The epidural space was identified using 16G sterile disposable Tuohy needle with hanging drop technique at L2- L3 interspace. Then 18G PORTEX epidural catheter was passed through the epidural needle in upward direction till about 4cms of the catheter was in the space. The needle was withdrawn, and the catheter was checked for intravascular and intradural by negative aspiration. Catheter was fixed after giving test dose of 3ml of Xylocaine 2%, to the back using adhesive tape. Then Patient induced with 5-7mg/kg of Thiopentone sodium ,2ug/kg fentanyl citrate and 0.1mg/kg of vecuronium bromide, Portex single lumen endotracheal tube was placed. The patients' lung was ventilated with 50% oxygen mixed with 50% nitrous oxide, maintained anesthesia with oxygen, sevoflurane and vecuronium bromide. Urinary catheterization was done. No narcotics were administered during the intraoperative period. After the operation finished, we extubated patients. Patient was shifted to postoperative ward and monitoring of HR, Blood pressure, oxygen saturation and Respiratory was done. In the postoperative period, when the patient first complained of pain, intensity of pain was assessed using VAS scale. When the VAS score was 4 or more, study drug was given epidurally.

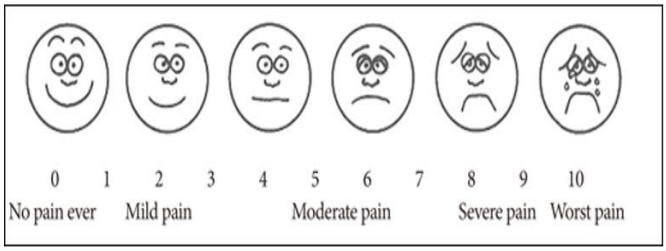
Group M- received morphine sulphate 2mg in 10ml Normal saline.

Group BM- received Bupivacaine hydrochloride 2ml (0.5%)10mg and Morphine sulphate 2mg diluted in Normal saline up to 10ml.

The intensity of pain and pain relief was assessed using VAS at 5, 10,15,30,60 minutes 2hours, and thereafter 2 hourly for 24 hours postoperatively. As and when the patient complains of further pain during the period of observation, intensity of pain was assessed again using VAS to know the effect of the study drug given earlier. If it was 4 or more, rescue analgesia was given in form of Inj. Diclofenac sodium 1.5 mg/kg intravenously slowly as per the ward protocol and the study would end at this stage. (provided RFT is normal).

Visual analog scale score

Visual analog scale (VAS) consisted of a 10 cm line, marked at 1cm each on which the patient makes a mark on the line that represents the intensity of pain he/she was experiencing. Mark '0' represents no pain and mark '10' represents worst possible pain. The numbers marked by the patient was taken as units of pain intensity.



VAS Score	Intensity of pain
0 – 2	No pain to slight pain
3 – 5	Mild pain.
6- 7	Moderate pain.
8 – 9	Severe pain.
10	Worst possible pain.

Observation and results

Onset of analgesia

Is the time interval from administration of the study drug (VAS>4) to first reduction in pain intensity by at least 10mm in VAS score.

Table 1

Onset of analgesia (min)	Group m (min)	Group bm (min)	p value
Mean ± sd	21.40±3.10	16.45±33.25	<0.0001

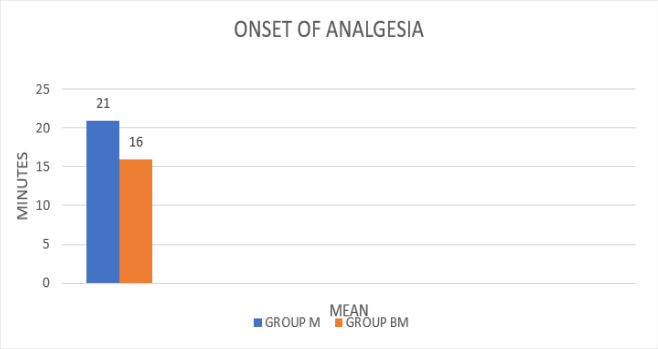


Figure 1

Mean Onset of analgesia in Group M was 21.40±3.10 minutes (MEAN±SD) and in Group BM *16.45±3.25* minutes (MEAN±SD).

Statistical analysis showed that onset of analgesia in group BM faster as compared to group M and statistically strongly significant with t=7.793 and p<0.0001.

Duration of analgesia

Is the time interval between onset of analgesia, till the patient complaints of pain (VAS>4) when rescue medication was given.

Table 2

DURATION OF ANALGESIA(HOURS)	GROUP M(HOURS)	GROUP BM(HOURS)	P VALUE
MEAN±SD	15.01±3.12	14.94±2.98	0.9089

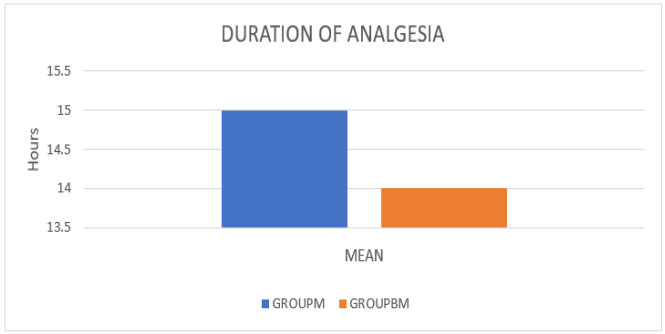


Figure 2

Table 3 shows Mean duration of analgesia in Group M was 15.01±3.12 hours (MEAN±SD) and in Group BM was 14.94±2.98 hours(MEAN±SD).

Statistical analysis showed that duration of analgesia was same in group M and Group BM, statistically not significant with t=0.1147 and p=0.9089.

Quality of analgesia

At the time at which rescue analgesia was given, the patient was asked to give a global assessment of the overall effectiveness of the analgesic treatment and it depends upon score 0 (no pain), 1(poor pain relief) ,2(fair pain relief), 3(good pain relief), 4(excellent pain relief)

Table 3

Pain Score	Group M	Group BM
0	-	-
1	2	-
2	7	4
3	33	32
4	8	14
MEAN±SD	2.88±0.71	3.18±0.59

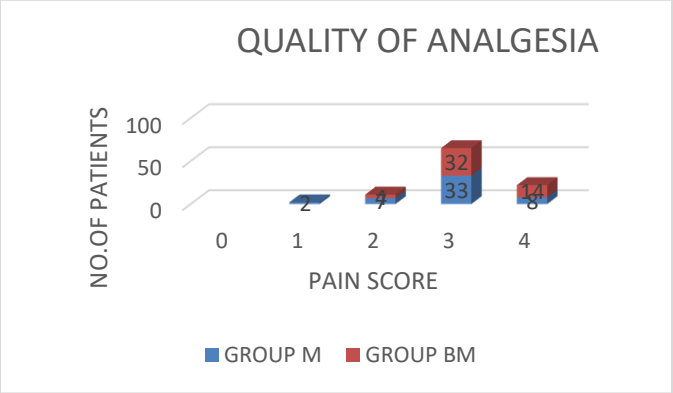
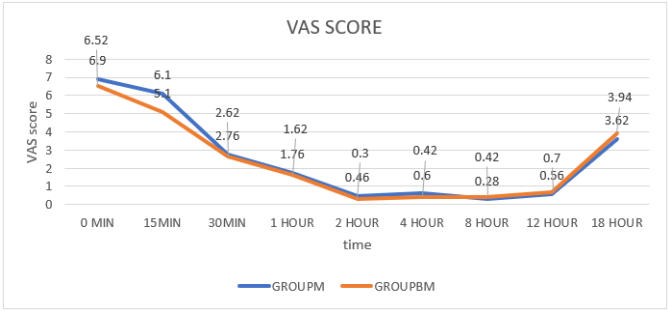


Figure 3

Statistically analysis showed that quality of analgesia better in Group BM, 14 patients in Group BM shows excellent pain relief. Statistically significant with p=0.0237 and t=2.2979.

VAS SCORE: observed in both groups at 0min,15min,30min,1 hour,2hour,4hour interval.

Figure 4



The difference in VAS score at 15 minutes in Group M score decrease to 6.15±1.05 and in Group BM score was 5.14±0.35 which was statistically extremely significant(p=0.0001).

Cardiovascular and respiratory effects

Comparison of HR, SBP and DBP in both groups.

Table 4

Time	Group M (Mean ± Sd)			Group BM (Mean ± Sd)		
	HR bpm	SBP mm Hg	DBP mm Hg	HR bpm	SBP mm Hg	DBP mm Hg
Base line	82.38±6.5	124.4±4.75	80.4±4.75	83.36±7.14	123.5±7.206	78.58±5.60
0 HR	75.1±5.38	119±6.46	72±6.41	78.84±6.249	118..64±9.927	76.52±7.294
1 HR	78.14±5.46	122±9.16	74.7±4.66	80.08±5.98	119.36±9.06	78.84±6.96
2 HR	77.3±6.26	117±7.84	73.7±5.24	78.83±5.24	119±7.35	75.78±4.98
4 HR	74.64±4.75	121.5.9±8.036	73.82±5.214	75.68±5.19	122.37±6.922	75.5±4.96
8 HR	74.26±5.241	121.4±6.356	74.3±6.021	76.28±5.004	122.68±5.84	76.46±4.95
12 HR	75.3±4.2	120±6.76	72.4±4.91	77.42±4.94	120.8±9.7	74.6±4.1
18 HR	76.2±6.7	121.3±7.006	74.1±5.59	78.18±5.27	124.88±6.671	76.02±5.45
24 HR	78.42.4±6.23	124.2±6.88	79.46±6.715	80.26±5.84	126.18.2±7.036	80.44±5.81

Figure 5

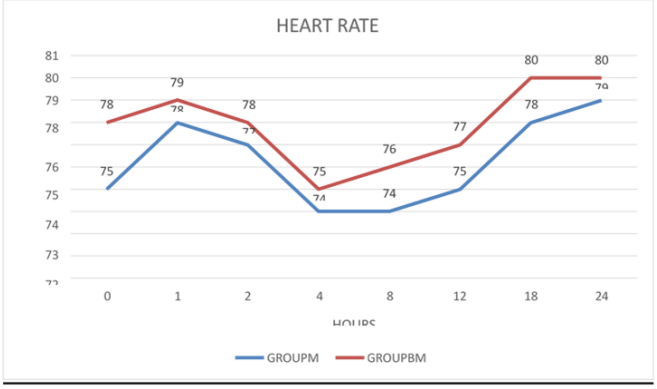


Figure 6

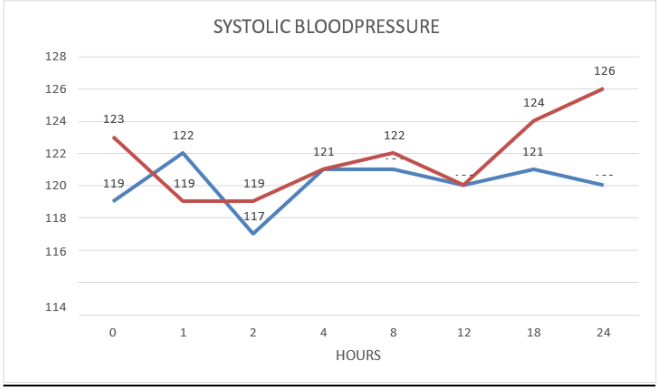
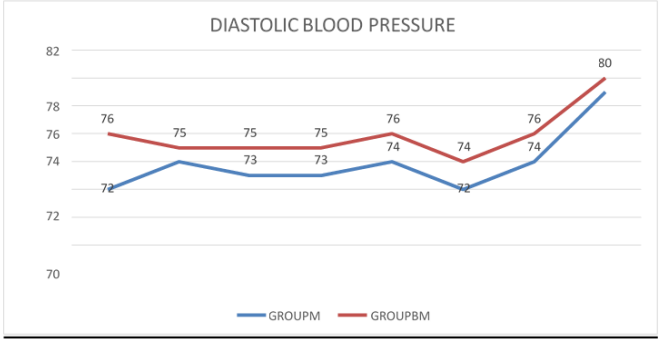


Figure 7



It can be seen from the above table that there were no differences in heart rate and blood pressure (both systolic and diastolic) between the two groups observed (p >0.05). Oxygen saturation and respiratory rate remains normal in all patients of both the group throughout the study period.

Adverse effects

Table 7

Adverse effects	Group m		Group bm	
	No	%	No	%
Nausea-Vomiting	7	14	3	6
Pruritus	6	12	3	6
Hypotension	1	2	2	4
Respiratory depression	0	0	0	0
Bradycardia	0	0	0	0

From the above chart, it can be Obser.

Pruritus was seen 6 patients (12%) of group M and 3 patients (6%) of group BM. insignificant (p>0.05)

Nausea and Vomiting were observed in 7 patients (14%) in group M and in 3 patients(6%) in Group BM (p>0.05)

Hypotension was seen in only 1 patient (2%) of Group M and in 2 Patients ofgroup BM. (p>0.05)

Respiratory depression and Bradycardia is not seen in any patient of both thegroups.

Discussion

Treatment of pain after surgery is central to the care of postoperative patients. Relief of pain and suffering is always has been one of the primaries aims of Anesthesiology practice. Postoperative pain is an unpleasant experience for the patient associated with number of physiological responses and many contribute to postoperative morbidity [10]. To maintain good quality of analgesia postoperatively is challenging task for the Anesthetist. This is partly due to fact that intensity of pain is extremely variable not only amongst patients but also with different surgical procedure. Regional Anesthesia is a safe, less expensive technique with advantage of prolonged pain relief [11]. To provide good pain relief during surgery and postoperative period is one of the important aspects of balanced anesthesia and epidural analgesia is its most important component. Pain is more severe on the first day after surgery and diminishes over

next 24 hours. And recedes slowly afterwards. Epidural analgesia considered by many as gold standard analgesic technique for major abdominal surgery. Other mode of analgesia like parenteral analgesia, even with patient-controlled delivery system, have limitations. Post operatively epidural analgesia helps in early mobilization of patient due to good pain relief. Sympathetic blockade provided by it helps in improved wound healing. Thrombo-embolic complication decreased due to attenuation of hypercoagulable response to surgery. The use of epidural opioids as adjuvants to local Anesthetic had become an increasingly popular technique for management of acute postoperative pain in recent times. It also provides dose sparing effect. Recent studies indicate that it is possible to achieve better analgesia with lower dose of opioid medication when these drugs are administered in extradural space as compared to intramuscular or intravenous route of administration. However, there are disadvantage associated with narcotics as they are not simple to use and associated with side effects.

The present study is a prospective randomized controlled clinical comparative study done to assess the efficacy and safety of epidural Morphine Sulphate versus epidural Bupivacaine hydrochloride plus Morphine sulphate for the management of postoperative pain in lower abdominal surgeries.

Following observations were recorded:

- Onset of analgesia.
- Duration of analgesia.
- Quality of analgesia
- Cardio- respiratory effects: Heart rate, blood pressure and respiratory rate.
- Adverse effects like pruritus, nausea, vomiting, respiratory depression and hypotension.

Onset of Analgesia

In our study, Majority of patients in group M had onset of analgesia between 16-20minutes whereas in group BM between 10-15 minutes. Statistical analysis showed that onset of analgesia was delayed in group M compared to group BM ($t=7.793$; $p< 0.0001$). VAS score at 15minutes in Group M was 6.15±1.05 and in Group BM was 5.14±0.35, difference was statistically extremely significant($p<0.0001$). We can correlate our study with the studies conducted by: Egon Lanz et al[12] reported that efficacy of epidural morphine is increased if morphine is given before the onset of pain, combination with local anesthetic doesn't interfere with efficacy and duration of epidural morphine. Tapan J. Parikh et al [1] reported that epidural morphine 0.1mg/kg plus bupivacaine (o.125%) had mean onset of analgesia was21.67±2.65minutes and epidural clonidine bupivacaine group had 15.17±2.22 min. this was statistically significant($p<0.05$). From above studies we can concluded that alone epidural morphine had mean onset of analgesia late than epidural morphine plus bupivacaine.

Duration of analgesia

In the present study, statistical analysis showed that duration of analgesia in both groups were same. Statistically was not significant ($t=0.1147$; $p=0.9089$). Our study is in agreement with the several studies. Ahmet Cosar [5] studied No. of doses required in epidural morphine 2mg group was 2.40±1.35 and in epidural morphine 2mg+bupivacaine 10mg 0.5% was 2.53±1.19 over 48hours postoperatively, statistically this difference was not significant ($p =0.792$). Varaprasad Raghupatruni et al [13] studied with 0.25mg/ml of morphine with 0.125%bupivacaine, duration of analgesia more with patient undergoing general surgery (4.75-4.8hr) compared to orthopedic surgery(4hr), duration of

analgesia depends upon dose, concentration, and type of surgery. Laxmi Pathak [2] reported that epidurally 1mg preservative free morphine and 2ml of 0.5% bupivacaine had average time to demand analgesic after last dose of epidural top up was 21.93hrs. morphine plus local anesthetic may or may not prolong the duration of post-operative analgesia as compared with morphine alone.

Quality of analgesia

Study shows that difference was statistically significant p=0.0237 t =2.29. Majority of patients expressed their analgesia as good to excellent. Y AduGyamfi [15] reported that epidural morphine 2mg with 4ml of 0.25% bupivacaine provides a safe and effective postoperative Analgesia. Dr. P. N. Jain et al [10] reported that continuous infusion of low dose morphine (0.007%) and bupivacaine (0.0625%) provides superior Analgesia at rest and during movement. Praveen Kumar Devulapalli et al[15] reported that quality of analgesia in epidural 2mg morphine was excellent in 50% patients, while in epidural butorphanol group 60% patients graded as excellent.

Cardiovascular and Respiratory effects

In the present study heart rate, blood pressure and respiratory rate remained stable throughout the observation period (table 5). 2 patients in group BM and 1 patient in group M had hypotension (fall in systolic BP <20% of basal reading) which was not statistically significant (p>0.05). Our study can be compared to the following studies: **Ahmet Cosar et al** [5]reported that in epidural morphine and epidural morphine plus bupivacaine group,no significant changes were observed in peripheral oxygen saturation and hemodynamic parameters HR, SBP, RR stable throughout period. P>0.05. **Dr P NJain et al** [10] with continuous infusion of epidural Morphine plus bupivacaine allvitals pulse, respiratory rate, BP normal throughout infusion period.

Adverse effects

Pruritus

A subjective unpleasant and irritating sensation that provokes an urgeto scratch and the symptoms typically start at the trunk, nose, around the eyes and is usually localized to facial areas, innervated by the trigeminal nerve. The spinalnucleus of the trigeminal nerve is rich in opioid receptors and is continuous with the substantia gelatinosa and Lissauer tract at C3-C4. The ophthalmic division of the spinal sensory nucleus of the trigeminal nerve is most inferior; thus, supporting the observation that the pruritus following neuraxial opioid administration is typically in the nose and upper part of the face (14). In our study 6 patients in group M had pruritus and 3 patients in group BM had pruritus which was statistically insignificant (p>0.05). **Egon Lanz et al** [12] reported occurrence of pruritus was more frequent in those who received 3mg morphine(p<0.05). **Oscar A.de Leon** [9] reported pruritus occurred in 22% patients(p<0.05) of whom 4% patient required therapy. **H. Jorgensen et al** [25] reported nine patients of epidural morphine bupivacaine group had itching(p=0.008)

Nausea and vomiting

It has been suggested that postoperative nausea and vomiting may be due to increased sensory or vagal input from the viscera or to stimulation of the chemoreceptor trigger zone either by the vestibular apparatus or by high concentration of opioid in plasma or cerebrospinal fluid (40). In our study 7 patients of Group M had nausea-vomiting whereas in Group BM 3 patients had nausea-vomiting, which was statistically insignificant(p>0.05). **Egon Lanz et al** [12] studied after dose of up to 5mg epidural morphine nausea andvomiting no more frequent than they were when no morphine was given. This side effect more frequent after dose of 8mg,10mg. **Oscar A.de**

Leon [9] studied with continuous infusion of epidural morphine (0.01%0+bupivavaine (0.05-0.1%) ,22% of patients experienced nausea-vomiting, most of episodes occurred duringthe first 24hour of surgery. ($p<0.05$)

Hypotension

In our study 1 patients of Group M and 2 patients of Group BM observed with hypotension. Which was statistically insignificant($p>0.05$) **Oscar De Leon et al** [9] reported hypotension occur in 3% (126) of his patients, out of which 90% (114) patients in thoracic epidural group and 10% (9) in lumbar epidural group. **Dr. P N jain et al** [10] reported there is no case of hypotension with low dose epidural morphine0.007% and bupivacaine0.0625%.

Respiratory depression and Bradycardia

Delayed respiratory depression isthe most troublesome of these side effects and appears to be largely responsible for the reluctance of anesthesiologists to use intrathecal or epidural narcotics. This phenomenon is thought to be due to transport of drug in cerebrospinal fluidfrom the lumbar region to the fourth ventricle, with consequent depression of the medullary respiratory centre. The incidence of delayed respiratory depression appears to be greatest with poorly lipid-soluble narcotic drugs. In our study, noneof the patient observed as respiratory depression ($p>0.05$). **Dr. P N jain et all** [10] reported, there is no case of respiratory depression with low dose epidural morphine0.007% and 0625%.

Conclusion

It can be concluded from the above study that Epidural Morphine sulphate along with Bupivacaine hydrochloride is safe, effective, and reliable method of postoperative pain relief with lesser side effects and greater patient satisfaction compared to epidural morphine alone. Bupivacaine hydrochloride with Morphine sulphate has rapid onset of analgesia so provide excellent analgesia in early postoperative period. Epidural analgesia also blunts the autonomic and somatic reflexes to pain and needs comparable small doses and low concentration of local anesthetic.

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