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Comparative evaluation of analgesic efficacy of morphine, bupivacaine and fentanyl along with local aesthetics for management of post-operative pain

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Abstract
Most patients who undergo surgical procedures experience acute postoperative pain, but evidence suggests that less than half report adequate postoperative pain relief. Many preoperative, intraoperative, and postoperative interventions and management strategies are available for reducing and managing postoperative pain. Hence based on the literature findings the current study was planned to evaluate the post-operative pain by administration of opioid analgesics, Morphine, Butorphanol and Fentanyl along with local Anaesthetic Bupivacaine, when given epidurally.
The 40 patients admitted to Department of Surgery and referred to department of Anaesthesia in IMS BHU, Varanasi from Jan 2016 to July 2016 for the epidural anaesthesia were included in the present study. Thepatients undergoing lower abdominal surgery and suitable for the epidural anaesthesia were included in the study.
From the above studies it can be conclude that Morphine or Butorphanol along with Bupivacaine can be safely given epidurally to obtain effective post-operative analgesia after lower abdominal surgeries. The duration of sedation is seen maximum in morphine administered patients. The Bupivacaine administered patients observed immediate onset of sedation. The maximum number of patients had seen the nausea and vomiting side effects in morphine group patients. In Bupivacaine administered patients are observed with hypotension as side effects prominently.

Keywords: opioid analgesics, morphine, butorphanol, fentanyl, local anaesthetic bupivacaine, epidural anaesthesia etc

Introduction
According to the American Society of Anaesthesiologist practice guidelines for acute pain management in the perioperative setting, acute pain is defined as pain present in a surgical patient after a procedure. The World Health Organization and International Association for the Study of Pain have recognized pain relief as a human right. Poorly managed postoperative pain can lead to complications and prolonged rehabilitation. Uncontrolled acute pain is associated with the development of chronic pain with reduction in quality of life. Appropriate pain relief leads to shortened hospital stays, reduced hospital costs, and increased patient satisfaction. As a result, the management of postoperative pain is an increasingly monitored quality measure. The Hospital Consumer Assessment of Health Providers and Systems (HCAHPS) scores measures patient satisfaction with in-hospital pain management and may have implications in regards to reimbursements [1].
Analgesia administered before the painful stimulus occurs may prevent or substantially reduce subsequent pain or analgesic requirements. This hypothesis has prompted numerous clinical studies, but few robust studies have clearly demonstrated its efficacy. Effective pre-emptive analgesic techniques use multiple pharmacological agents to reduce nociceptor activation by blocking or decreasing receptor activation, and inhibiting the production or activity of pain neurotransmitters. Pre-emptive analgesia can be administered via local wound infiltration, epidural or systemic administration prior to surgical incision. A meta-analysis of randomized trials reported patients receiving pre-emptive local anesthetic wound infiltration and nonsteroidal anti-inflammatory administration experience a decrease in analgesic consumption, but no decrease in postoperative pain scores. Pre-emptive epidural analgesia did show a decrease in pain scores as well as analgesic consumption. Pre-emptive local anesthetic injection around small laparoscopic port incision sites was not effective in terms of managing postoperative visceral pain [2]. Overall, pre-emptive analgesia may offer some short-term benefits, particularly in ambulatory surgery patients.
Despite years of advances in pain management, the mainstay of postoperative pain therapy in many settings is still opioids. Opioids bind to receptors in the central nervous system and peripheral tissues and modulate the effect of the nociceptors. They can be administered via oral, transdermal, parenteral, neuraxial, and rectal routes. The most commonly used intravenous opioids for postoperative pain are morphine, hydromorphone (dilaudid), and fentanyl. Morphine is the

standard choice for opiates and is widely used. It has a rapid onset of action with peak effect occurring in 1 to 2 hours. Fentanyl and hydromorphone are synthetic derivatives of morphine and are more potent, have a shorter onset of action, and shorter halflives compared with morphine.

All opioids have significant side effects that limit their use. The most important side effect is respiratory depression that could result in hypoxia and respiratory arrest. Hence, regular monitoring of respiration and oxygen saturation is essential in patients on opioids postoperatively. In addition, nausea, vomiting, pruritus, and reduction in bowel motility leading to ileus and constipation are also common side effects of these medications. Longer-term use of opioids can lead to dependence and addiction. Once the patient is able to tolerate oral intake, oral opioids can be initiated and continued after discharge from the hospital. With the development of enhanced recovery protocols, particularly in colorectal surgery, primarily opioid-based regimens are being challenged by other agents and approaches to postoperative pain management [3].

Most patients who undergo surgical procedures experience acute postoperative pain, but evidence suggests that less than half report adequate postoperative pain relief. Many preoperative, intraoperative, and postoperative interventions and management strategies are available for reducing and managing postoperative pain. Hence based on the literature findings the current study was planned to evaluate the post-operative pain by administration of opioid analgesics, Morphine, Butorphanol and Fentanyl along with local Anaesthetic Bupivacaine, when given epidurally.

Methodology

The 40 patients admitted to Department of Surgery and referred to department of Anaesthesia in IMS BHU, Varanasi from Jan 2016 to July 2016 for the epidural anaesthesia were included in the present study. The patients undergoing lower abdominal surgery and suitable for the epidural anaesthesia were included in the study.

The approval of the institutional ethics committee was taken before starting the study. All the patients and their parents were informed consents. The aim and the objective of the present study were conveyed to them.

The following was the administration protocol for study groups:

- Control group: 1ml Normal saline (0.9%) + 9 ml (0.125%) Bupivacaine
- Morphine group: 1 ml Morphine sulphate (3mg) preservative free + 9 ml (0.125%) Bupivacaine
- Bupivacaine group: 1 ml Butorphanol tartrate (2 mg) + 9 ml (0.125%) Bupivacaine
- Fentanyl group: 1 ml Fentanyl citrate (50 mg) + 9 ml (0.125%) Bupivacaine

The other drugs given to all the patients in common were 0.5% Bupivacaine 2-3 ml – for spinal Anaesthesia and Inj. Midazolam (2-3mg) –Intravenously as pre-Anaesthetic medication.

Inclusion criteria: Adult patients of either sex of ASA I OR II, falling between the age groups of 20-65 years presenting for surgery under spinal anaesthesia were included after obtaining a written informed consent.

Exclusion criteria: Patients with history of asthma; cardiac or hepatic disorders; Taking centrally acting drugs like antidepressants; Diminished mental competence, deafness, visualdisturbances which would prevent them tocomprehend the Visual analogue scale (VAS); Pregnant or lactating mothers.

Results & Discussion

The total 40 patients undergone the lower abdominal surgery and suitable for the epidural anaesthesia werecollected and presented as below. The patients were administered 4 different dose of the analgesics as mentioned above.

Table 1: Age distribution

Age	Control group	Morphine group	Bupivacaine group	Fentanyl group	Total
20-30 years	6	7	6	8	27
31-40 years	2	3	3	1	9
41-50 years	2	0	1	1	4
Total	10	10	10	10	40

Table 2: Onset & Duration of Analgesia

Age	Control group	Morphine group	Bupivacaine group	Fentanyl group
Onset (mins)	11.2 – 18.9	8.3 -10.5	4.3 – 6.1	2.1 – 3.5
Duration mins)	108.5 – 142.5	1230 – 1463	485 – 690	273 - 379

The Control group administered showed slow onset and Fentanyl administered group shows fastest onset. The duration of the analgesia is seen maximum in morphine administered patients.

Table 3: Onset & Duration of Sedation

Age	Control group	Morphine group	Bupivacaine group	Fentanyl group
Onset (mins)	26.3 – 29.6	11.4 – 17.5	7.6 – 11. 3	7.3 – 12.2
Duration (mins)	91 -105	250 – 318	148 – 209	105 - 163

The duration of sedation is seen maximum in morphine administered patients. The Bupivacaine administered patients observed immediate onset of sedation. The maximum number of patients had seen the nausea and vomiting side effects in morphine group patients. In Bupivacaine administered patients are observed with hypotension as side effects prominently.

Table 4: Side Effects

Age	Control group	Morphine group	Bupivacaine group	Fentanyl group	Total
Nausea & Vomiting	1	2	1	1	5
Respiratory depression	0	0	0	0	0
Hypotension	1	2	2	1	6

The VAS score for butorphanol was lower at time 2 as opposed to fentanyl at the same time point. It was also noted that butorphanol had a relatively lower VAS score at time 3 as opposed to fentanyl. This indicates that butorphanol is capable

of reducing the pain better than fentanyl as similar results were seen by Thakore *et al*. [4] Furthermore in our study we also observed that there were around 36.7% of the patients in the butorphanol group needed a rescue analgesic when compared to fentanyl which was 6.7% in contrast to the results obtained by Thakore *et al.* [4]

Claxton *et al.* conducted further study on postoperative pain relief over the fentanyl and found that the incidence of nausea and vomiting after discharge was higher in morphine than in fentanyl group [5]. A similar study done by Wajima *et al*. which compared the effect of I.V butorphanol against brachial plexus administration showed the same adverse effects like nausea, vomiting and slight drowsiness and they too, were not significant [6].

In our study the equi-analgesic activity of both butorphanol and fentanyl, although similar, butorphanol has an edge over fentanyl due to its favourable safety profile. Conclusions from other studies also indicate that butorphanol and fentanyl have similar efficacy profile for postoperative analgesia. In fact, Butorphanol has remarkable analgesic affect and other effects like antistressor, sedative and anti shivering effect [7]. Postoperative pain gives rise to varied physiological and biological phenomena. Minimizing postoperative pain leads to, earlier mobilization and discharge from hospital, thus aiding recovery. Most of the opioid receptor agonists could bring about required postoperative. A rapid and effective analgesic is sought for postoperative pain. Opioids are the choice for severe pain but limited by the plentiful adverse effects.

Effective post-operative analgesia decreases morbidity, which allows early ambulation and discharge. Pain relief may involve administration of analgesic drugs by various routes and/or non-pharmacological techniques. Out of all these measures, epidural administration of local Anaethetics, combination of local Anaethetics and opioids or combination of local Anaethetics and other adjuvants are proved to be very effective in providing good post-operative analgesia. The discovery of spinal opioid receptors has paved a new way to extend the duration of analgesia offered by spinal analgesics in the post- operative period with reduced doses of local Anaethetics and avoiding prolonged residual motor paralysis. The addition of small doses of opioids has made this possible, at the same time avoiding their potential side effects which are commonly seen with their use by other routes i.e. IM, IV for post operative pain relief.

Conclusion

From the above studies it can be conclude that Morphine or Butorphanol along with Bupivacaine can be safely given epidurally to obtain effective post-operative analgesia after lower abdominal surgeries.

The duration of sedation is seen maximum in morphine administered patients. The Bupivacaine administered patients observed immediate onset of sedation. The maximum number of patients had seen the nausea and vomiting side effects in morphine group patients. In Bupivacaine administered patients are observed with hypotension as side effects prominently.

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