ORIGINAL RESEARCH

Effectiveness of Post-Operative Analgesia with Epidural Tramadol, Fentanyl and Buprenorphine

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ABSTRACTS

Introduction: Pain is a more dreadful ruler over humanity than death. Postoperative pain management is crucial for providing rapid relief from pain after surgery. This can be achieved by the use of several methods such as systemic analgesics (either orally or parenterally), epidural analgesia, local infiltration at the surgical site, and local nerve blocks. Epidural pain relief with local anaesthetic drugs is a widely used, straightforward, efficient, and cost-effective method of delivering pain relief after surgery.**Material and Methods:**This study was a future comparative randomised study undertaken in the anaesthesia department of tertiary care institutions in Haldia. Following permission from the ethics committee, a total of 100 patients who were scheduled to undergo elective procedures on their lower limbs or lower abdomens were enrolled in the study. The inclusion criteria included of patients who were classified as ASA I and II, aged between 18 and 45 years, and included both male and female individuals.**Results:**The distribution of weight was similar in all three groups. The beginning of pain relief was quicker in the Fentanyl group compared to the other two groups, and this difference was statistically significant (p = 0.000). The time it took for pain relief to start in the Buprenorphine group was substantially longer compared to the other two groups, according to statistical analysis (p = 0.000). The length of pain relief was longest in the Buprenorphine group, and this difference was statistically significant compared to the other groups (p=0.000). The length of pain relief was the shortest in the fentanyl group, which was statistically significant when compared to the other groups (p=0.000). The number of doses was lowest in the Buprenorphine group, followed by the Tramadol group, which required less doses than the Fentanyl group. G. Ozalp, F. Guner and coworkers (1998) conducted a study to assess the effectiveness and safety of patient-controlled epidural analgesia using morphine or fentanyl in combination with Bupivacaine for relieving postoperative pain. They determined that both approaches were successful in pain prevention, although due to less adverse effects, Fentanyl might be considered more favourable than Morphine.**Conclusion:**The current investigation indicates that the quality of pain relief was similar among the three medicines. Fentanyl has the quickest onset of pain relief, but because it doesn't last as long as tramadol and buprenorphine, it needs to be administered more often. Buprenorphine has a longer duration of pain relief and hence requires fewer dosages compared to tramadol and fentanyl.

Keywords: Post Operative Analgesia, Epidural Tramadol, Fentanyl, Buprenorphine

INTRODUCTION

Pain is a more dreadful ruler of humanity than death.[1]The taxonomy committee of the International Association for the study of pain defines pain as "A disagreeable sensory and emotional experience linked to real or potential harm to tissues or described in relation to such harm."[2]Pain, being a subjective experience, is only felt by the person experiencing it. When it comes to reporting the pain, patients are particularly variable and untrustworthy in terms of their symptoms.[2]The combined spinal and epidural anaesthesia technique (CSEA) is a regional anaesthesia technique that combines the advantages of spinal anaesthesia and epidural anaesthesia and analgesia.[3]Postoperative pain management is crucial for rapid pain reduction after surgery. This can be achieved by the use of several methods such as systemic analgesics (taken orally or injected), epidural analgesia, local infiltration at the surgical site, and local nerve blocks. Epidural pain relief with local anaesthetic drugs is a widely used, straightforward, efficient, and cost-effective method of delivering pain relief after surgery. Because local anaesthetics only last for a short period of time, opioids have been used

to ensure that even modest amounts can offer strong pain relief for a satisfactory duration while minimising adverse effects.[4]Post-surgery pain relief using bupivacaine through the caudal epidural route is well-established for surgeries below the belly button in children.[5,6]The average length of surgical pain relief afforded by bupivacaine is restricted.[7]Various medications like tramadol, fentanyl, clonidine, and midazolam in combination with bupivacaine extend the duration of pain relief after surgery. Tramadol is a pain reliever that works by acting on opioid receptors in the central nervous system.[8]The primary location where epidurally injected fentanyl has its effects is the substantia gelatinosa, which is located on the dorsal horn of the spinal cord.[9]Post-surgery pain is seen as a type of immediate pain caused by the surgical procedure, which leads to inflammation and the start of a nerve response. It is a collection of various uncomfortable sensory, emotional, and mental sensations caused by the surgical trauma and linked to autonomic, endocrine-metabolic, physiological, and behavioural reactions. Although there have been improvements in understanding the mechanisms behind pain, the use of pain-relieving medications, and the development of better procedures, patients still often feel significant pain following surgery.[10]Post-surgery pain has caught the interest of many individuals as it is one of the most uncomfortable results of any surgical procedure, and its elimination gives significant relief to the patient.[4]In the past, opioids and NSAIDs have been administered in many ways to offer adequate pain relief after surgery. However, all of these methods have their own limitations and disadvantages.[11]Epidural analgesia is a secure treatment for relieving postoperative pain and is comparable to conventional techniques of pain relief.[12]Epidural analgesia is often regarded as the preferred analgesic treatment for major surgery.[6]Patients can recover and return to their daily activities more quickly with epidural analgesia compared to parenteral opioids.[13]Opiates that have a stronger attraction to the receptor sites will result in a longer period of pain relief.[14]Epidural morphine (preservative-free version) has been widely employed for pain relief after surgery. It is considered one of the preferable opioids due to its extended duration of effect at a low dose. Nevertheless, numerous adverse reactions like queasiness, throwing up, itchiness, difficulty urinating, and delayed breathing problems have been documented.[15]

MATERIAL AND METHODS

This study was a future comparative randomised study undertaken in the anaesthesia department of tertiary care institutions in Haldia. Following permission from the ethics committee, a total of 100 patients who were scheduled for elective procedures on their lower limbs or lower abdomen were enrolled in the study. The inclusion criteria included of patients who were classified as ASA I and II, aged between 18 and 45 years, and included both male and female individuals. Exclusion criteria included patients with ASA physical status III and above, pregnant individuals, patients with uncontrolled hypertension, procedures involving the bladder, patients who refused the anaesthetic approach, and those with contra-indications to regional anaesthesia. All the patients underwent a comprehensive clinical examination as part of the preanesthetic evaluation, and standard laboratory tests were performed. They were informed about the study and the anaesthesia method. A proper, documented, and well-informed consent was obtained for the same. All the patients were instructed not to eat or drink anything after 10pm on the day before surgery. They were given a tablet of Alprazolam 0.25mg at 10pm on the night before surgery and a tablet of Ranitidine 150mg at 7am on the day of surgery, along with little sips of water. Sixty patients were assigned randomly to three groups using computer-generated random numbers through a simple randomization process. A total of 150 envelopes were used, each containing the treatment allotment organised in a random order. When a patient was included in the trial, an envelope was opened in sequential order from a predefined pack of envelopes. The envelope was opened right before the surgery began. The patients and the investigator documenting the impact were unaware of which medicine was being given to each patient. The double blinding approach was employed to eliminate bias. The patients were separated into three groups as follows; Group T: Tramadol group (n=50), Group F: Fentanyl group (n=50), Group B: Buprenorphine group (n=50). In the room before the surgery, all the patients were evaluated again on the day of the operation. An intravenous line was established using an 18G IV cannula and ringer lactate solution was initiated. A combination spinal epidural procedure was conducted on each patient, following all necessary aseptic precautions. The patient was seated and an 18G epidural needle was inserted into the gap between the L2 and L3 vertebrae. The epidural space was located using a procedure that involved identifying a decrease of resistance, and then an 18G epidural catheter was inserted into the space. A test dose of 3ml of Xylocaine with adrenaline (2% concentration, with a ratio of 1:200000) was administered to check for the correct insertion of the epidural catheter, ruling out any placement in the spinal canal or blood vessels. A subarachnoid block was carried out in the L3 – L4 area using a 25G spinal needle and 15mg of injection.Bupivicaine 0.5% concentrated. Analgesics were not given during the surgery, and the patient was moved to the postoperative ward once the surgery was over. In the postoperative ward, when the patient expressed discomfort, various measurements were taken to assess their condition, including pulse rate, blood pressure, breathing rate, and VAS score (0hrs). Next, patients in Group T were given additional doses of tramadol injection at a concentration of 1mg/kg

diluted with 10ml of distilled water whenever they had discomfort within 24 hours following the initial treatment. Patients in Group F were administered further doses of fentanyl 1µg/kg using spinal top ups, which were diluted to 10ml using distilled water, if they had discomfort within a 24-hour period starting from the initial dose. Patients in Group B were given further doses of buprenorphine at a concentration of 3µg/kg diluted with 10ml of distilled water whenever they experienced discomfort within 24 hours of the initial dosage. The pain severity and alleviation after injecting the medication into the epidural space were evaluated using the Visual Analogue Scale (VAS), which ranges from 0 (no pain) to 10 (worst imaginable pain). The beginning of pain relief, length of pain relief, and frequency of further doses were also observed.

RESULT

Table 1 Demographic distribution, onset of analgesia and duration of analgesia in study.

Age (in years)	Group T	Group F	Group B	GpT-GpF	GpT-GpB	GpB-GpF
	36.60±9.82	34.25±9.42	37.15±8.98	0.706	0.686	0.320
Weight(Kgs)	56.5±6.98	60.8±7.52	58.6±7.32	0.150	0.462	0.368
Onset of analgesia(mins	8.263±0.68	4.046±0.69	14.923±1.98	0.000	0.000	0.000
Duration of analgesia(mins	436.23±36.23	236.28±20.12	1102.5±28.2	0.000	0.000	0.000
Number of doses	5.0±0.0	7.2±0.9	3.0±0.0	_	_	_

Table 1 displays the distribution of age, while the distribution of weight was similar across all three groups. The beginning of pain relief was quicker in the Fentanyl group compared to the other two groups, and this difference was very significant from a statistical standpoint (p = 0.000). The time it took for pain relief to begin in the Buprenorphine group was considerably longer compared to the other two groups, according to statistical analysis (p = 0.000). The length of pain relief was longest in the Buprenorphine group, and this difference was statistically significant when compared to the other groups (p=0.000). The length of pain relief was the shortest in the fentanyl group, which was statistically significant when compared to the other groups (p=0.000). The number of doses was lowest in the Buprenorphine group, followed by the Tramadol group, which required less doses than the Fentanyl group.

	Group T(n=50)	Group F(n=50)	Group B(n=50)
0 hr	1.9	02	02
1 hr	-	-	-
2 hrs	-	-	-
3 hrs	-	0.9	-
4 hrs	-	0.5	-
5 hrs	-	-	-
6 hrs	0.58	0.6	-
7 hrs	0.78	0.8	-
8 hrs	0.5	0.5	-
9 hrs	-	0.3	-
10 hrs	-	0.56	-
11 hrs	-	0.5	-
12 hrs	0.45	0.6	-
18 hrs	0.8	0.9	02
24 hrs	-	--	-

Table 2 displays that the average VAS score was below 1 in all the groups within the 24-hour period following the initial administration of the epidural top up.

Table-2: Comparison of side effects between the groups.

	GROUP T	GROUP F	GROUP B
Nausea and Vomiting	10	6	4
Hypotension	-	-	-
Resp. depression	-	-	-
Urinary retention	2	-	6
Pruritis	-	5	-

In this study, Nausea & Vomiting was seen in 10 patients from the Tramadol group, 6 patients from the fentanyl group, and 4 patients from the buprenorphine group. Urinary retention was seen in two patients in the Tramadol group and six patients in the Buprenorphine group. There were no cases of urinary retention seen in the Fentanyl group in the current investigation. It was noticed that pruritis occurred in the present investigation, although only in 5 individuals from the fentanyl group. There were no patients who had itching in the Tramadol & Buprenorphine group. Hypotension and respiratory depression were not found in any group of individuals.

DISCUSSION

Despite advancements in perioperative care, significant surgical procedures are still accompanied by consequences such as discomfort, organ impairment, and extended recovery. It is believed that adequate pain treatment can enhance the results of surgery by reducing complications, the need for hospitalisation, and the time needed for recovery. There is a general agreement that effective pain relief is necessary for a speedy postoperative recovery.[16]TakekazuTerai, HidekazuYukioka et al (1993) conducted a study on pain treatment after surgery using either lumbar epidural or intramuscular buprenorphine in 31 patients undergoing hepatectomy. When patients initially reported pain following surgery, either 0.06 mg or 0.12 mg of buprenorphine was given in either 10ml or 20ml of saline solution through the epidural route. Alternatively, 0.12 mg was supplied intramuscularly. Epidural buprenorphine at a dose of 0.06 mg in 20ml saline and intramuscular buprenorphine at a dose of 0.12 mg both resulted in inadequate pain relief. An epidural injection of buprenorphine, either 0.12 mg in 10ml or 20ml of saline, resulted in full pain relief lasting around 10 hours. There were no notable alterations over time in respiratory and circulatory factors caused by buprenorphine. None of the patients had any significant ill effects. They advocate using a diluted solution of buprenorphine 0.12 mg in 10 to 12 ml of saline for lumbar epidural injection to provide postoperative pain relief after hepatectomy.[17]Choi PT, Bhandari M & colleagues (2003) conducted a clinical trial on patients who were having hip or knee replacements. They evaluated the use of postoperative lumbar epiduro analgesia with other types of pain treatment. The researchers found that individuals who received epidural analgesia had lower pain scores than those who received systemic analgesia for pain alleviation during activity after surgery. The advantages are greater in the initial postoperative phase.[18]Sawhney S, R.C.Gupta et al (2004) conducted a prospective, randomised trial to assess the effectiveness of Bupivacaine, Morphine & Ketamine administered in the epidural area, in different combinations, in 60 postoperative patients. The researchers determined that administering a mixture of Ketamine and Morphine in the epidural region is highly effective in providing pain relief after surgery. The combination of these medications provides much superior pain relief and lasts longer compared to when each drug is used alone. There was also no alteration in the occurrence and the arrangement of problems. Therefore, they suggested using Ketamine (0.5 mg/kg) along with morphine (0.05 mg/kg) administered epidurally for postoperative pain relief.[19]S.A. Lytle, D.M. Gold Smith and colleagues (1991) conducted a retrospective study on 134 patients who were given continuous epidural Fentanyl for postoperative pain relief. Patients were given continuous epidural infusions for 24 to 72 hours after surgery using a dosage of 5 mg/ml of Fentanyl. The side effects were either fewer than or similar to those of epidural morphine. Side effects did not occur in 70.6% of the people examined. This evidence indicates that epidural Fentanyl offers effective pain management with few negative effects. Jeffray A. Grass, Neal T. Sakima and his team (1997) carried out a randomised double-blind study to compare the effects of epidural Fentanyl and Sufentanil analgesia following caesarean delivery. Eighty women having a caesarean section were randomly divided into groups to receive either Fentanyl or Sufentanil through epidural administration. The doses of Fentanyl ranged from 25 to 200 mg, while the doses of Sufentanil ranged from 5 to 31 mg. Each group consisted of 10 women. The medication was given to relieve postoperative pain. Pain was evaluated using visual analogue scales (VAS 0 – 100 mm). They proposed that the comparative pain-relieving strength of epidural S:F is around 5 and that there were no distinctions between the opioids in terms of the start, length, and effectiveness of pain relief when equal pain-relieving doses are given following lidocaine anaesthesia for caesarean delivery. G. Ozalp, F. Guner and coworkers (1998) conducted a study to assess the effectiveness and safety of patient-controlled epidural analgesia using morphine or fentanyl in combination with Bupivacaine for relieving postoperative pain. They determined that both approaches were successful in pain prevention, however due to less adverse effects, Fentanyl would be considered a better option than Morphine.[20]Michele Curatalo, Thomas W. Schnider& colleagues (2000) used an optimisation model (direct search) to determine the best combination of bupivacaine dose, fentanyl dose, clonidine dose, and infusion rate for continuous postoperative epidural analgesia. A total of twenty combinations were examined. The optimisation process results in a decrease in the occurrence of side effects and the average pain scores. The top three combinations of Bupivacaine dose (mg/L), Fentanyl dose (mg/L), clonidine dose (mg/L), and infusion rate (ml/L) were: 9-21-5-7, 8-31-0-9, and 13-25-0-9, respectively. They determined that these three combinations might be the best ones to offer pain

relief following a significant abdominal surgery.[21]Premila Malik, ChhaviManchanda, and Naveen Malhotra (2006) conducted a study to evaluate and compare the safety and effectiveness of postoperative pain relief with epidural butorphanol and fentanyl. The study was prospective, randomised, and double-blind. 60 individuals were randomly split into two groups, A and B, with 31 people in each group. Group a received epidural butorphanol 2 mg, whereas group B received epidural fentanyl 50 mg. The recorded data included the timing of additional dosages, the time between injections, and the overall amount of analgesic medicine administered within a 24-hour period. They determined that both butorphanol and fentanyl are efficient and secure medications for postoperative epidural pain relief with minimal adverse effects.[22]Koshy.T, Afzal.L, and Kaur.B (1994) conducted a study where they compared the effects of epidural morphine and epidural buprenorphine for postoperative pain relief using a double-blind approach. They compared 4 milligrammes of epidural morphine with 0.12 milligrammes of epidural buprenorphine for postoperative pain relief. All the patients were monitored for 48 hours after surgery and evaluated for the start, length, and strength of pain relief as well as any adverse effects. Both medications showed strong pain-relieving effects by significantly reducing the pain score according to Magill's categorization. The onset of effect was nearly the same for both medications, although buprenorphine demonstrated a statistically significant longer duration of activity. The occurrence of adverse reactions was also significantly lower following buprenorphine. Therefore, they concluded that buprenorphine is superior than morphine since it has a longer duration of action and minimal side effects.[23]Yasuko Miwa, EijiYonemura et al (1996) examined the impact of epidural buprenorphine on the minimum olveolar concentration (MAC) of volatile anaesthetics, the length of time pain relief lasts, and respiratory function throughout the perioperative period. The researchers determined that administering 4 mg/kg of buprenorphine through an epidural gave long-lasting pain relief when employed as a preventive measure. Additionally, this approach resulted in a decrease in anaesthesia during surgery and the need for pain medication after the operation, with the reduction being dependent on the dosage. D. Kumar, N Dev, and N Gupta (1997) conducted a comparative analysis of epidural Buprenorphine and Ketamine for alleviating postoperative pain. The researchers found that while both medications provided pain relief without any notable adverse effects, the pain relief from 31 mg of Ketamine was short-lived and unpredictable, whereas 0.15 mg of Buprenorphine offered longer-lasting and higher-quality pain relief. Abdul Hakim, A.M.Hashia et al (2007) carried out a study comparing epidural morphine and buprenorphine for pain relief after surgery. A total of one hundred patients were evenly split into two groups to receive either 0.12 mg of buprenorphine (group 1) or 2 mg of morphine (group 2) by epidural administration for pain management. Patients were monitored for 24 hours after surgery to assess the time it took for pain relief to begin, how long it lasted, and how effective it was, as well as any potential side effects of these medications. Both medications demonstrated substantial pain alleviation. The onset of pain relief was the same for both medicines, but buprenorphine had a much longer duration of effect compared to morphine. The occurrence of adverse reactions was lower with buprenorphine in comparison to morphine. It was determined that epidural buprenorphine for pain relief after surgery lasts longer and has fewer negative effects compared to morphine. Pinky Rathie, R S Verma and colleagues (1998) demonstrated in their research on the use of epidural tramadol for postoperative pain treatment that it can provide sufficient, secure, and long-lasting analgesia after surgery. Sahar Siddik-Sayyid, Marie Aouad-Maroun and their team (1999) conducted a study to examine the pain-relieving effects of 100mg versus 200mg of epidural tramadol and saline in patients who were having an elective caesarean section. It was discovered that epidural tramadol 100mg can effectively relieve postoperative pain without causing breathing problems in patients following a caesarean delivery.[24]Paul S Myles, Sally Troedel et al (1999) did a study on the pain visual analogue scale to determine if it exhibits a linear or non-linear relationship. They examined 52 patients who had undergone surgery and assessed the level of pain they experienced using the Visual Analogue Scale (VAS). They have demonstrated that the Visual Analogue Scale (VAS) is a linear measurement tool for assessing acute mild to moderate pain in postoperative patients. Modifications in the VAS score indicate a proportional alteration in the intensity of pain.[25]

CONCLUSION

The current investigation indicates that the quality of pain relief was similar among the three medicines. Fentanyl has the quickest onset of pain relief, but because it doesn't last as long as tramadol and buprenorphine, it needs to be administered more often. Buprenorphine has a longer duration of pain relief and hence requires fewer dosages compared to tramadol and fentanyl. However, the time it took for pain relief to begin was longer with buprenorphine. Tramadol also provided a comparable level of pain relief, with the time it took for the pain relief to start and how long it lasted being similar to fentanyl and buprenorphine. The detected side effects were not concerning. The hunt for a suitable opioid for epidural administration to give postoperative pain management is currently ongoing, with the introduction of newer opioids that have fewer adverse effects. With the implementation of infusion pump in the postoperative

ward, additional studies can focus on patient controlled analgesia and continuous epidural analgesia. Butorphanol and Tramadol, two synthetic nonnarcotic opioid analgesics, offer effective pain relief after surgery when administered epidurally as the only medications. The length of pain relief was greater with Tramadol compared to Butorphanol, while the effectiveness of pain relief was higher with Butorphanol compared to Tramadol. However, both medicines have similar adverse effects except for sedation, which is more pronounced with Butorphanol.

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