

Epidural Infusion of Bupivacaine with Morphine for Pain Relief after Renal Transplantation: A Comparison with PCA Intravenous Morphine

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ABSTRACT

Background: The postoperative pain management is one of the important factor for a successful outcome after kidney transplantation. Intravenous opioids provide the mainstay of analgesia following renal transplantation. With the increasing use of epidural anaesthesia for renal transplantation surgery, continuous epidural analgesia might be an alternate choice for postoperative pain management in transplant patients. Our study was to compare the quality of analgesia, the incidence of side effects, and patient's overall satisfaction after renal transplant surgery between IV PCA and continuous epidural analgesia.

Patients & methods: This prospective study included 40 adult patients ASA II-III undergoing living related elective renal transplantation surgery. Group I received general anaesthesia followed by postoperative IV PCA morphine 0.1 mg.kg⁻¹ loading dose followed by 1 mg bolus dose with lockout period of 10 minutes. Group II received combined spinal epidural anaesthesia followed by continuous epidural bupivacaine 0.0625%+1.5 mg morphine 10ml hr⁻¹. The observed parameters were assessment of pain by VAS, total dose of bupivacaine & morphine, sedation score, the incidence of side effects and patient's overall satisfaction.

Results: Pain relief was better at rest and during movement ($p < 0.05$) in the continuous epidural group. The mean dose of morphine was 35±5.26 mg including bolus doses in Group I, while in Group II it was 9.8±1.38 mg and bupivacaine dosage was 262±36.82 mg. Nausea/vomiting was the major side effect observed in group-I. Majority of patients rated their pain relief as "good".

Conclusion: Continuous epidural infusion of bupivacaine with morphine provides better quality of analgesia with fewer side effects compared to PCA with intravenous morphine.

KEYWORDS : IV PCA morphine, Epidural Bupivacaine with Morphine, Renal transplantation surgery

Renal transplantation is considered as the treatment of choice for patients with end stage renal disease.¹ Perioperative consideration for renal transplantation surgery requires selection of drugs with minimal toxicity to the patient and graft, maintenance of vital functions and adequate pain relief. In majority of cases intravenous opioids are the mainstay of analgesia in these patients. With increasing use of regional anesthesia for renal transplantation surgery, epidural analgesia might become an alternative choice for post operative pain management.

The aim of this prospective nonrandomized study was to compare the quality of postoperative analgesia, the incidence of side effects & patient's overall satisfaction.

PATIENTS AND METHODS

After receiving approval of the ethics committee and informed consent from the patients, 40 adult patients undergoing

living related renal transplant were enrolled between January 2007 - June 2007. On the day prior to operation patients were explained about the mode of anaesthesia and made familiar with visual analogue score (VAS) for pain assessment. Patients in group 1 received general anaesthesia and were offered intravenous patient controlled analgesia (IV PCA) with morphine as post operative analgesia. Patient in group 2 had regional (combined spinal epidural) anesthesia and were given 0.0625% bupivacaine with morphine for post operative analgesia. All patients in group 1 were made familiar with patient controlled analgesia (PCA) pump. On the day of operation, prior to surgery all patients received unheparinized hemodialysis. Post-hemodialysis electrolytes, hemogram, platelet count, coagulation profile and electrocardiogram were obtained. Intraoperatively monitoring with ECG, Pulse oxymetry, NIBP, CVP, ETCO₂, temperature and urine output was carried out in both groups. In group 1 general anaesthesia was induced

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with intravenous fentanyl (2 µg.kg⁻¹) and thiopental (5 mg.kg⁻¹). Atracurium was used (0.5 mg.kg⁻¹) to facilitate intubation as well as to provide muscle relaxation during surgery. Maintenance was done by mixture of nitrous oxide with oxygen & isoflurane and intermittent fentanyl. Mechanical ventilation was adjusted to maintain ETCO₂ between 32-38 mmHg. Residual neuromuscular block was reversed at the end of surgery with neostigmine (0.05 mg.kg⁻¹) and glycopyrolate (4 µgkg⁻¹) and trachea extubated in OR when acceptable criteria were met.

In group 2 combined spinal epidural anaesthesia was given by double space technique. Epidural space was located by LOR technique at L2-3 space with 18 gauges Tuohy needle and epidural catheter was inserted 7cm inside the space. Spinal anaesthesia given by 23 gauge spinal needle (B-Brawn), between L3-4 interspace and 0.5% hyperbaric bupivacaine (15.5-17.5 mg) was injected. Intermittant midazolam 1.0 mg was used for conscious sedation as and when required and oxygen was administered by a face mask throughout surgery. The first epidural 14-18 ml bolus of mixture of 0.5% bupivacaine and 2% lignocaine with adrenaline was administered 60 minutes later, this was followed by 5-7 ml top up doses every hourly till the completion of surgery. Postoperatively, all patients were shifted to ICU and analgesic regime was started within 30 minutes of patient's arrival.

Group-I patients received loading dose of morphine (0.1 mg.kg⁻¹) intravenously. The PCA syringe pump (Graseby Medical Ltd, UK, 3300) was programmed to deliver morphine 1 mg bolus with a lockout interval of 10 minute without background infusion and limit of 30mg in 8 hours. Patients were instructed to use the PCA morphine as needed to achieve comfort at rest and on movement. In group-II patients, continuous infusion of 0.0625% bupivacaine with 1.5 mg. morphine prepared in 50 ml syringe with normal saline was started at rate of 10 ml/ hour. Subsequently, infusion rate was increased by 2 ml when VAS =4 or decreased by 2 ml when VAS was <4 or when patient developed motor weakness. Motor blocked was evaluated in terms of modified 4 grade Bromage scale. (0=no weakness, 1=inability to raise extended legs (just able to move knees and feet), 2=inability to flex knee (able to move feet or first digit only), 3=inability to move any joints in legs. No rescue analgesic was used in both groups. The following information was collected for 48 hours. Assessment of pain was done with 0-10 cm VAS at rest (0=no pain and 10= worst possible pain) at 4 hourly interval and VAS during movement at 8 hourly interval for 48 hours, and clinical neurological evaluation was done twice daily. Patients were evaluated by sedation score. 0= wide awake, 1= mildly sleepy and responsive to verbal command, 2=

moderately sleepy, 3= extremely sleepy and unresponsive to nociceptive stimulation. Side effects like nausea, vomiting, pruritus; hypotension, sedation and respiratory depression were also recorded. Patient's satisfaction was judged as good (VAS=4 and no side effects), fair (VAS 5-7 and minimal side effects) or unsatisfactory (VAS >7 and severe side effect). Total dose of bupivacaine and morphine used was recorded.

All data are expressed as mean ± SD. Statistical analysis was done with the unpaired t-test and p value <0.05 was considered significant.

RESULTS

The recipient's demographic characteristics are shown in Table-1. Both the groups were similar with respect to demographic parameters like age, gender, weight and duration of haemodialysis HD.

VAS was significantly lower in group II, both at rest and during movement (p<0.05) (Figure 1,2).

Mean morphine consumption was significantly lower in group 2 than in group 1 (Table-2). The bupivacaine consumption was 262±36.82mg. 3 patients experienced lower limb weakness (grade-2) requiring decrease in infusion rate.

All patients in group-I were mildly sedated (sedation score=1). Hypotension and respiratory depression didn't occur in either group. Incidence of nausea and vomiting was significantly higher in PCA than in epidural group

Table 1
Patient characteristics (Mean±SD)

	Group-1(n=20)	Group-2(n=20)
Age (Years)	38.75 ± 10.8	38.7 ± 9.4
Gender (M/F)	18:2	19:1
Weight (Kg.)	55.4 ± 4.2	54.5 ± 5.5
Duration of HD (Months)	26.65 ± 14.1	26.85 ± 10.9

Table 2
Analgesic Dose

	Group 1 (n=20)	Group 2 (n=20)
Morphine(mg)	35 ± 5.26	9.8 ± 1.38
Bupivacaine(mg)		262 ± 36.82

P<0.05

Table 3
Side-Effects

	Group-1 (n=20)	Group-2(n=20)
Nausea, Vomiting	40%	15%
Pruritus	0	20%
Hypotension	0	0
Respiratory depression	0	0

P<0.05

Table 4
Patients overall satisfaction

	Group- I	Group – II
Good	84 %	72%
Fair	9 %	17%
Unsatisfactory	7%	11%

P<0.05

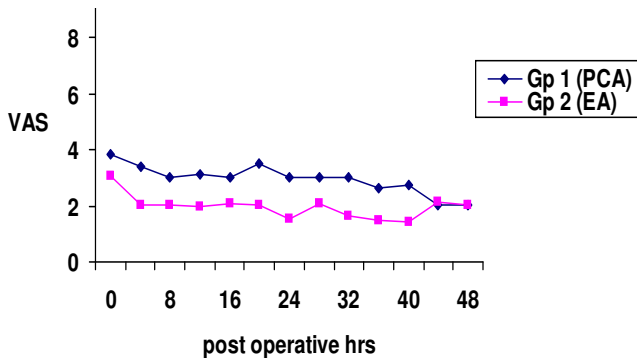


Figure 1
VAS at rest

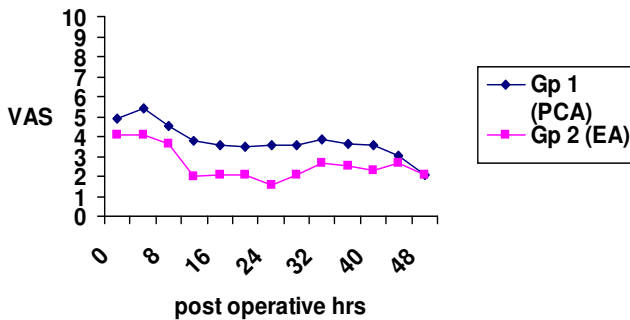


Figure 2
VAS during movement

(p<0.05). Epidural group was associated with high incidence of pruritus (20%) (Table 3).

The majority of patients rated their analgesia as “good”. The respective % for the EPI and PCA group were 84% and 72% (p>0.05). There was no difference between the groups with regard to overall satisfaction rating.

DISCUSSION

Patients undergoing renal transplantation suffer from many co-morbid conditions like hypertension, coronary artery disease, diabetes, and acid-base and electrolyte imbalance. A careful selection of analgesic drugs and method of analgesia are required. To date, studies of pain management following renal transplantation have not recommended any special agent or technique. Majority of

renal transplants are performed under general anaesthesia due to theoretical risk of epidural hematoma and cardiovascular instability, and IV PCA-morphine provides the mainstay of analgesia as demonstrated in a survey carried out at 27 NHS renal transplant units in UK². With increasing use of continuous epidural anaesthesia since last one and half decade for renal transplantation surgery, epidural analgesia may be a better option for pain relief in these patients. Hence, we compared these two techniques of analgesia in these high risk patients.

Proper selection of analgesic drug is important because typical hemodynamic and biochemical changes of kidney transplant recipients may influence the pharmacokinetic profile of drugs.³ In addition, delayed graft function or decreased creatinine clearance in the immediate postoperative period may further affect the excretion of drugs. There is no concrete knowledge of risks or benefits of morphine use via epidural route in patients with renal disease, however, the impact of intravenous morphine on kidney has been studied.⁴ Recently Pauli-Magnus and his colleagues have added further concern by their work documenting the accumulation of morphine-3-glucuronide metabolite also.⁵ Despite these, morphine has been used for analgesia without any apparent problems. We have not measured plasma levels of morphine and its metabolites but we found that morphine consumption was lower than the preset maximum in PCA group probably due to accumulation of potent metabolites which may have acted in a negative feedback loop to limit PCA use by the patient. Also being a live related transplantation, none of our patients had delayed graft function in the immediate postoperative period which might have decreased concentration of morphine and its metabolites.

The safety of bupivacaine for lumbar epidural anaesthesia has been studied in renal transplantation by Hammouda et al; they found no higher plasma concentrations with epidural administration of bupivacaine in uraemic patients compared to nonuraemic patients⁶ We selected to use 0.0625% bupivacaine in group II because using lower concentration has less effect on blood pressure which is crucial for early function of the transplanted kidney. It also allows us to detect neurological complications in the postoperative period related to uraemic bleeding tendency. We did not observe hypotension or neurological complications related to epidural catheterization during the postoperative period. Three patients developed motor weakness despite lower concentration of bupivacaine which responded to decrease in infusion rate.

Quality of analgesia was better with epidural group compared to IV-PCA group and VAS reading was lower in the early postoperative period when pain is intense.

Several studies have shown superior pain relief with epidural analgesia compared to IV PCA with opioids after major surgeries^{7,8,9} due to a potential to reduce or eliminate physiological stress response, reduce alteration of cardiovascular, pulmonary and gastrointestinal physiology, ensure better cognitive function and improve outcome. Combination of small concentration of local analgesic and opioid provides better pain relief than either drug used alone by blocking sympathetic as well as somatic nervous system activation limiting the side-effects of individual drug. Epidural opioids may provide nearly complete analgesia at rest but suboptimal relief on movement. Our data confirm that epidural analgesia using opioid with local analgesic is highly effective in reducing movement associated pain. Despite better pain relief in epidural group, there was no significant difference in overall patient's satisfaction regarding their pain therapy indicating that satisfaction does not correlate with pain relief measured with VAS.

The higher incidence of nausea, vomiting and sedation in PCA group was related to higher requirement of morphine. Nausea and vomiting can be prevented by prophylactic use of antiemetic. Pruritus is most common side-effect of epidural opioids. It is known to be central in origin but its exact mechanism is not clear. In our study, 20% patients in epidural group had pruritus which was not troublesome. Respiratory depression or hypotension did not occur in either group in our study which supports safety of PCA and epidural analgesia in chronic renal failure patients.

We conclude that continuous epidural infusion of bupivacaine with morphine in renal transplant recipient is associated with better quality of analgesia with fewer side effects compared to patient controlled analgesia with intravenous morphine.

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