

Comparison of the postoperative analgesia of intravenous infusion of adenosine and fentanyl

Sir,

Postoperative pain is distressing for the patients. The postoperative pain makes patient immobile, making him

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vulnerable to deep venous thrombosis, pulmonary atelectasis, muscle wasting and urinary retention.^[1]

One modality for relief of postoperative pain is by giving intravenous infusion of adenosine. The potential of adenosine as a non-narcotic analgesic in anaesthetized patients has been explored in clinical trials and observed that intraoperative infusion of adenosine stabilizes hemodynamic parameters and reduces the requirement for anaesthesia and analgesics during surgery.^[2]

In the present study, analgesic effects of adenosine and fentanyl were compared in first 24 hours with following parameters:

- Pain score calculated by visual analog scale
- FLACC (Face, Legs, Activity, Cry, Consolability) behavior pain scale to assess quality of analgesia^[3]
- Postoperative requirement for morphine
- Hemodynamic parameters like pulse and blood pressure (BP)
- Sedation scale score and
- Adverse effects

Twenty patients who were undergoing elective surgeries under spinal anaesthesia with heavy bupivacaine (0.5%) like abdominal hysterectomy (adenosine $n = 4$, fentanyl $n = 6$), hernia (adenosine $n = 2$, fentanyl $n = 1$), fractures (adenosine $n = 1$, fentanyl $n = 1$), laparotomy (adenosine $n = 1$), gluteal mass excision (adenosine $n = 1$), vaginal hysterectomy (adenosine $n = 1$, fentanyl $n = 1$), Freyer's prostatectomy (adenosine $n = 1$) were selected in this study.

The study population included patients of either sex, aged between 18 and 65 years, American Society of Anaesthesiologists (ASA) I and II patients. Patients excluded from this were: ASA III and IV patients, patients with cardiac arrhythmia, severe hepatic and renal impairment.

This study was approved by Institutional Ethics Committee. This study was performed in accordance with the declaration of Helsinki. After obtaining written informed consent from each patient, the patients were randomly assigned to one of the study groups. Randomization was done with the help of randomization software (Rando 1.2, 2004). Drug was given by one investigator and follow-up was done at every two hours for the total period of 24 hours by another investigator who was blinded. Postoperative level of anaesthesia was noted and when the sensory level receded two segments, solutions of adenosine or fentanyl were infused to the patients with the help of infusion pumps.^[3] Adenosine in the dose range of 4-50 $\mu\text{g/kg/min}$ and fentanyl 1 $\mu\text{g/kg/h}$ was given as intravenous infusion over the period of 20 minutes. Then both the syringes were refilled by non-blinded observer, adenosine with normal

saline and fentanyl syringe with fentanyl solution. Infusions were given for a total period of 24 hours.

Patients were observed for pulse, BP, pain, sedation and FLACC behavior pain scale scores every 2 hours for period of 24 hours. Rescue analgesic, intravenous morphine 1 mg or more was given when pain score was more than 3. Maximum dose of morphine was limited to 10 mg in 24 hours.^[4]

Statistical analysis was carried out by using unpaired *t*-test between the two groups. *P* values <0.05 were considered statistically significant.

Significantly higher pain and FLACC behavior scale score were observed with fentanyl at 2 hours as compared to adenosine 15-50 $\mu\text{g/kg/min}$ [Table 1]. Fentanyl and adenosine 15-50 $\mu\text{g/kg/min}$ had shown significantly less FLACC behavior scale scores at 8 hours as compared to adenosine 4-6 $\mu\text{g/kg/min}$ [Table 1]. Patients with adenosine 15-50 $\mu\text{g/kg/min}$ were more or less comfortable during the first 8 hours of study, whereas fentanyl group patients were more comfortable after 12 hours as observed with FLACC scale. Fukunaga *et al.* (2003) also observed significantly reduced pain scores in their study with adenosine.^[5]

Morphine requirement was more with adenosine 15-50 $\mu\text{g/kg/min}$ as compared to fentanyl [Table 2]. Peri-operative infusion of adenosine 50-500 $\mu\text{g/kg/min}$ was associated with decreased opioid requirement and reduced postoperative pain complaints.^[2,5]

There was no significant difference observed in sedation scores at all the observation periods in all groups.

Adenosine in the dose of 25-50 $\mu\text{g/kg/min}$ was found useful for opioid-sparing effect, as two patients, one of abdominal hysterectomy and another of vaginal hysterectomy in this dose range did not require morphine at all. This has proved prolonged analgesic effect of adenosine at lower dose in Indian patients than the doses (166-500 $\mu\text{g/kg/min}$) used in other studies.^[5,6]

Limitation of this study is that other analgesics were required apart from morphine in some of the patients for relieving pain [Table 2]. Variable-rate infusion was used in this study as it decreases the possibility of untoward hemodynamic effects like sinus arrest and severe hypotension,^[6] and also may be helpful for finding dose in Indian patients.

Adenosine has longer lasting antinociceptive effect in postoperative period. Opioid-sparing effect of adenosine is observed even in the dose 25-50 $\mu\text{g/kg/min}$ is useful for postoperative analgesia. Higher dose of adenosine 50-100 $\mu\text{g/kg/min}$ can be used as an alternative to narcotics for

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Table 1: Changes in pulse, BP, VAS and FLACC behavior pain scale with adenosine and fentanyl

Parameter	Drug given	Time in hours						
		0	2	4	8	12	20	24
Pulse	Adenosine 4-6 µg/kg/min	72.5±19.2	83.75±18.87	88.25±21.23	84±19.04	78.75±18.2	74.5±11.7	76±12.54
	Adenosine 15-50 µg/kg/min	81.16±18.24	81.16±17.61	83.83±11.97	84.33±11.75	88.66±10.25*	85.33±12.04	81.66±6.97
	Fentanyl 1 µg/kg/h	79.55±11.69	85.55±11.83	88.77±11.27	88.55±15.97	82.33±10.5	87.22±9.94	85.55±8.55
Systolic blood pressure	Adenosine 4-6 µg/kg/min	120.5±15	135±12.7	138±17.2	142±5.25	135±5.77	137±9.45	129±9
	Adenosine 15-50 µg/kg/min	119.66±8.64	117.5±13.41	120.83±11.77 [‡]	126.66±16.32 ^{‡‡}	126.66±16.32 ^{‡‡}	123.33±8.16 [‡]	123.66±7.52 [‡]
	Fentanyl 1 µg/kg/h	141.55±12.95	133.55±19.93	135.22±10.08 [‡]	132.33±9.75 ^{‡‡‡}	132.33±8.90 ^{‡‡}	131±7.03 [‡]	131±7.88 [‡]
Diastolic blood pressure	Adenosine 4-6 µg/kg/min	69.75±9.25	80.5±6.55	89.5±11	85.25±5.5	85±5.77	88.5±8.69	83.5±7.89
	Adenosine 15-50 µg/kg/min	69±10.43	72±7.72	74.5±8.09	76.16±10.2	76.5±10.5	73.66±8.04	73.33±8.16
	Fentanyl 1 µg/kg/h	88.55±9.95	81.44±10.69	83.66±8.93 ^{‡‡}	82.55±5.12 ^{‡‡}	82.11±5.17 ^{‡‡}	81.55±6.25 ^{‡‡‡}	81.77±6.65 [‡]
Pain score	Adenosine 4-6 µg/kg/min	1.5±2.38	3.25±4.27	3.5±2.08	3±1.41	1.5±1.29	1.75±2.21	0.75±0.5
	Adenosine 15-50 µg/kg/min	0.16±0.41	0.16±0.41 ^{***}	1.5±1.64	1±1.3	1.16±1.16	0	0 ^{‡‡}
	Fentanyl 1 µg/kg/h	1.88±1.49	3.33±1.33	1.22±1.19 [‡]	0.77±1.25 [‡]	0.11±0.31 ^{‡‡}	0 [‡]	0 ^{‡‡‡}
FLACC behavior pain scale	Adenosine 4-6 µg/kg/min	0.75±1.5	2.5±3	1.75±2.36	1.5±1.29	0.5±1	0.5±1	0
	Adenosine 15-50 µg/kg/min	0	0*	0	0.16±0.41 [‡]	0.16±0.41	0	0
	Fentanyl 1 µg/kg/h	0.33±0.67	1.33±1.39	0.11±0.31 [‡]	0.22±0.63 [‡]	0	0	0

^{‡/‡‡/‡‡‡}P<0.05, ^{**/‡‡‡/‡‡‡‡}P<0.01, ^{***/‡‡‡‡/‡‡‡‡‡}P<0.001; *Adenosine 15-50 µg/kg/min versus fentanyl 1 µg/kg/h, [‡]Adenosine 4-6 µg/kg/min versus fentanyl 1 µg/kg/h, [‡]Adenosine 4-6 µg/kg/min versus adenosine 15-50 µg/kg/min; BP=Blood pressure; VAS= Visual analog score; FLACC=Face, legs, activity, cry, consolability

Table 2: Rescue analgesic requirement with adenosine and fentanyl

Drug group	Analgesic needed in 24 hours	Per patient requirement (Mean±SD)	P value
Adenosine 4-6 µg/kg/min	Morphine 16 mg [‡] Diclofenac 300 mg	4±2.16	0.087 (Adenosine 4-6 µg/kg/min Vs Adenosine 15-50 µg/kg/min)
Adenosine 15-50 µg/kg/min	Morphine 9 mg [‡] Tramadol 100 mg	1.5±1.87	0.41 (Adenosine 15-50 µg/kg/min Vs Fentanyl)
Fentanyl 1 µg/kg/h	Morphine 22 mg [‡] Diclofenac 75 mg [‡] Tramadol 100 mg	2.2±1.39	0.085 (Adenosine 4-6 µg/kg/min Vs Fentanyl)
Time of morphine administration			
	0-4 hrs	4-12 hrs	12-24 hrs
Adenosine 4-6 µg/kg/min	7 mg	7 mg	0
Adenosine 15-50 µg/kg/min	2 mg	5 mg	2 mg
Fentanyl 1 µg/kg/h	18 mg	4 mg	0

postoperative pain. Narcotics has certain limitations for their use like need for license, stocking arrangement, storage responsibility, misuse of narcotics, hence adenosine can be used as an alternative to morphine or narcotics drugs.

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