Sir,

Postoperative pain is distressing for the patients. The postoperative pain makes patient immobile, making him
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 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 \(\mu\)g/kg/min [Table 1]. Fentanyl and adenosine 15-50 \(\mu\)g/kg/min had shown significantly less FLACC behavior scale scores at 8 hours as compared to adenosine 4-6 \(\mu\)g/kg/min [Table 1]. Patients with adenosine 15-50 \(\mu\)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 \(\mu\)g/kg/min as compared to fentanyl [Table 2]. Peri-operative infusion of adenosine 50-500 \(\mu\)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 \(\mu\)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 \(\mu\)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 \(\mu\)g/kg/min is useful for postoperative analgesia. Higher dose of adenosine 50-100 \(\mu\)g/kg/min can be used as an alternative to narcotics for
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±18.47 | 88.25±11.23 | 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 | 86.66±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±15.25 | 135±7.77 | 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±7.77 | 88.5±8.69 | 83.5±7.89 |
|           | Adenosine 15-50 µg/kg/min | 69±10.43 | 72.7±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 |

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.

Yogendra Keche, Radha Yegnarayan,
Adnanal Sarkar∗, Shalini Thombre†

Departments of Pharmacology, and ¹Anaesthesia,

Smt Kashibai Navale Medical College and Hospital, Narhe, Pune, Maharashtra, India

Address for correspondence:
Yogendra N. Keche, Department of Pharmacology, Smt Kashibai Navale Medical College and Hospital, OFF Pune-Bangalore Westerly bypass highway, STES Narhe Campus, Narhe Ambegaon, Pune, Maharashtra, India. E-mail: drynkeche@gmail.com
REFERENCES

1. Chaturvedi S, Chaturvedi A. Postoperative pain and its management. Indian J Crit Care Med 2007;11:204-11.
2. Segerdahl M, Ekbom A, Sandelin K, Wickman M, Sollevi A. Perioperative adenosine infusion reduces the requirement for isoflurane and postoperative analgesics. Anesth Analg 1995;80:1145-9.
3. Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: A behavioral scale for scoring postoperative pain in young children. Pediatr Nurs 1997;23:293-7.
4. Segerdahl M, Irestedt L, Sollevi L. Antinociceptive effect of perioperative adenosine infusion in abdominal hysterectomy. Acta Anaesthesiol Scand 1997;41:473-9.
5. Fukunaga AF, Alexander GE, Stark CW. Characterization of analgesic actions of adenosine: Comparison of adenosine and remifentanil infusions in patients undergoing major surgical procedures. Pain 2003;101:129-38.
6. Zarate E, Sa Rego MM, White PF, Duffy L, Shearer V, Griffin JD, et al. Comparison of Adenosine and Remifentanyl Infusions as Adjutants to Desflurane anesthesis. Anesthesiology 1999;90:956-63.

Announcement

Android App

A free application to browse and search the journal’s content is now available for Android based mobiles and devices. The application provides “Table of Contents” of the latest issues, which are stored on the device for future offline browsing. Internet connection is required to access the back issues and search facility. The application is compatible with all the versions of Android. The application can be downloaded from https://market.android.com/details?id=comm.app.medknow. For suggestions and comments do write back to us.