ORIGINAL RESEARCH PAPER

Anaesthesiology

COMPARATIVE ANALGESIC EFFICACY OF INTRAVENOUS IBUPROFEN, PARACETAMOL AND THEIR COMBINATION IN SPINE SURGERY: A RANDOMIZED DOUBLE BLINDED COMPARATIVE STUDY

KEY WORDS: Ibuprofen; Paracetamol; Spine Surgery; Postoperative Pain

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ABSTRACT

Background: Multimodal analgesia reduces opioid exposure after spine surgery. Evidence on combined intravenous ibuprofen and paracetamol remains limited. **Objective:** To compare intravenous paracetamol, ibuprofen and their combination for postoperative analgesia in spine surgery. **Methods:** This randomized double blinded comparative study included 60 adults allocated equally to paracetamol plus saline, ibuprofen plus saline or ibuprofen plus paracetamol. The first dose was administered 15 minutes before induction and repeated every 8 hours for 24 hours. Pain scores, morphine use, fentanyl use, PONV and adverse effects were recorded. **Results:** Pain scores differed significantly at all time points. At 8 hours, VAS scores were 51.5 ± 8.13, 37.0 ± 7.33 and 20.0 ± 3.24 respectively. Morphine consumption was lowest with the combination (7.55 ± 5.16 mg; $p < 0.0001$). No monitored adverse effects occurred. **Conclusion:** Combined intravenous ibuprofen and paracetamol provided superior early analgesia and reduced opioid requirement.

INTRODUCTION

Postoperative pain remains a major clinical concern after surgery because it affects recovery, mobilisation, respiratory function and patient satisfaction. Contemporary perioperative pain guidance supports individualized pain plans and multimodal analgesia rather than reliance on opioids alone (Chou et al., 2016; Gan, 2017). Spine surgery produces incisional, muscular, osseous and neural pain stimuli. Early pain may be intense and may increase opioid exposure when nonopioid analgesics provide inadequate coverage (Yoo et al., 2019).

Paracetamol provides central analgesia through prostaglandin modulation and additional serotonergic and endocannabinoid mechanisms. It has clinical utility in perioperative care and has a favourable bleeding profile at therapeutic doses (Anderson, 2008). Ibuprofen is a nonselective NSAID that inhibits cyclooxygenase enzymes and reduces prostaglandin mediated nociceptor sensitization. Perioperative use of intravenous NSAIDs can reduce opioid demand as part of multimodal analgesia (Cashman, 1996; Smith, 2011).

Akbas et al. (2021) described lower postoperative pain and morphine consumption with intravenous ibuprofen compared with intravenous paracetamol after lumbar disc surgery. That trial did not assess the combined use of both drugs. The present study compared intravenous paracetamol, intravenous ibuprofen and their combination for postoperative analgesia in spine surgery.

MATERIALS AND METHODS

This randomized double blinded comparative study was conducted in the Department of Anaesthesiology, School of Medical Sciences and Research, Sharda Hospital, Greater Noida from April 2024 to November 2025. The procedures followed in the study were in accordance with ethical standards for human research. Ethical clearance was obtained from the Institutional Ethics Committee and the study was registered with the Clinical Trials Registry India under CTRI/2025/02/080883. Written informed consent was obtained from each participant before enrolment.

Adult patients aged 18 to 60 years, of either sex, with ASA physical status I to III and scheduled for spine surgery under general anaesthesia were eligible. Patients with contraindications to either study drug, relevant drug allergy, significant hepatic or renal dysfunction, bleeding disorder, pregnancy, chronic opioid use or inability to use the pain scale were excluded.

Sixty patients were randomized by a computer generated chart into three equal groups of 20 patients. An independent anaesthesiologist prepared the study drugs and did not participate in patient management or data collection. Patients and investigators remained unaware of group allocation. Group PS received intravenous paracetamol 1 g in 100 ml and 100 ml normal saline every 8 hours. Group IS received intravenous ibuprofen 400 mg in 100 ml and 100 ml normal saline every 8 hours. Group IP received intravenous ibuprofen 400 mg and intravenous paracetamol 1 g every 8 hours through separate intravenous lines. The first dose was administered 15 minutes before induction and the regimen continued for 24 hours postoperatively.

All patients received standard monitoring. Anaesthesia was induced with propofol, fentanyl and vecuronium and was maintained with oxygen, nitrous oxide and sevoflurane. An intraoperative rise in heart rate or systolic blood pressure above 20% of baseline was treated with fentanyl 25 microgram boluses. Ondansetron 4 mg was administered before extubation. Postoperatively, patients received morphine through a patient controlled analgesia pump at 0.5 mg/ml with 1 ml boluses on demand and a lockout interval of 7 minutes.

The primary outcome was postoperative pain measured with a 0 to 100 visual analogue scale at 0, 2, 6, 8, 12 and 24 hours. The visual analogue scale is an accepted method for acute postoperative pain assessment (Myles et al., 2017). Secondary outcomes included 24 hour morphine consumption, intraoperative fentanyl consumption during the first 4 hours, PONV score, hemodynamic parameters and adverse effects. Categorical variables were summarised as number and percentage. Continuous variables were summarised as mean ± SD or median with interquartile range according to distribution. ANOVA, Kruskal Wallis test, Chi square test or Fisher exact test was used as appropriate. A p value below 0.05 was considered statistically significant.

Results

Sixty patients were randomized and analysed, with 20 patients in each group. Baseline demographic variables were comparable across groups. Duration of surgery differed

significantly and was longest in the combination group. This imbalance was retained in interpretation because longer surgery would be expected to increase postoperative pain rather than reduce it.

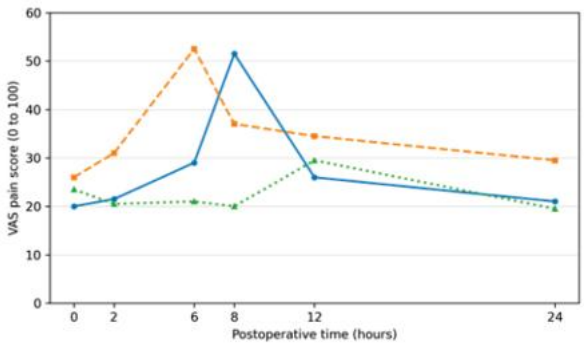
Table 1. Baseline Demographic and Clinical Characteristics.

Characteristic	PS (n = 20)	IS (n = 20)	IP (n = 20)	p value
Age, years	44.55 ± 13.73	43.70 ± 13.12	48.15 ± 9.83	0.485
Male sex, n (%)	10 (50)	9 (45)	10 (50)	0.935
BMI, kg/m²	23.03 ± 4.26	23.48 ± 5.38	22.70 ± 3.66	0.861
ASA class I, n (%)	20 (100)	20 (100)	20 (100)	NA
Duration of surgery, min	230.25 ± 13.13	237.00 ± 9.23	240.00 ± 0.00	0.005

Values are mean ± SD unless otherwise stated. PS = paracetamol plus saline; IS = ibuprofen plus saline; IP = ibuprofen plus paracetamol.

Postoperative pain scores differed significantly among groups at every measured time point. The combination group showed the lowest pain scores at most intervals. At 8 hours, the mean VAS score was 20.0 ± 3.24 in IP compared with 51.5 ± 8.13 in PS and 37.0 ± 7.33 in IS. The pain score trend is shown in Figure 1.

Figure 1. Postoperative VAS Pain Score Trend Over 24 Hours.



VAS = visual analogue scale. PS = solid line, paracetamol plus saline; IS = dashed line, ibuprofen plus saline; IP = dotted line, ibuprofen plus paracetamol.

Table 2. Postoperative Pain, Opioid Use and Adverse Events.

Outcome	PS (n = 20)	IS (n = 20)	IP (n = 20)	p value
VAS 0 h	20 ± 4.59	26 ± 5.98	23.5 ± 5.87	0.004
VAS 2 h	21.5 ± 4.89	31 ± 5.53	20.5 ± 3.94	<0.0001
VAS 6 h	29 ± 3.08	52.5 ± 5.5	21 ± 4.47	<0.0001
VAS 8 h	51.5 ± 8.13	37 ± 7.33	20 ± 3.24	<0.0001
VAS 12 h	26 ± 5.98	34.5 ± 8.26	29.5 ± 2.24	0.0002
VAS 24 h	21 ± 4.47	29.5 ± 5.1	19.5 ± 2.24	<0.0001
Morphine, mg	20.00 ± 2.20	25.00 ± 2.51	7.55 ± 5.16	<0.0001
No extra fentanyl, n (%)	1 (5)	0 (0)	7 (35)	0.0009
50 mcg fentanyl, n (%)	5 (25)	7 (35)	0 (0)	0.0009
PONV and monitored adverse effects	Absent	Absent	Absent	NA

Values are mean ± SD unless otherwise stated. PONV and monitored adverse effects included bradycardia, hypotension, respiratory depression, urinary retention and pruritus.

Total morphine consumption showed a large difference across groups. Consumption was lowest in IP at 7.55 ± 5.16 mg and highest in IS at 25.00 ± 2.51 mg. Intraoperative fentanyl use also differed significantly. No patient in IP required 50 microgram fentanyl and 35% required no additional intraoperative fentanyl. PONV was absent in all patients across all time intervals. No bradycardia, hypotension, respiratory depression, urinary retention or pruritus was observed.

DISCUSSION

This randomized double blinded comparative study showed that combined intravenous ibuprofen and intravenous paracetamol provided better postoperative analgesia than either agent alone in patients undergoing spine surgery. The combination group had lower pain scores at most postoperative time points, lower morphine consumption and lower intraoperative fentanyl use. No increase in PONV or monitored opioid related adverse effects was observed.

Akbas et al. (2021) reported that intravenous ibuprofen reduced postoperative pain and morphine consumption compared with intravenous paracetamol after lumbar disc surgery. The present study extends that observation because the combined regimen was tested directly and showed lower opioid requirement than ibuprofen alone. Shimia et al. (2014) showed the utility of intravenous paracetamol as an adjunct analgesic after lumbar discectomy. The PS arm in this study had acceptable early pain scores at 0 and 2 hours but pain increased at 8 hours. This pattern suggests that paracetamol alone may not provide sufficient coverage during the middle postoperative interval in this setting.

Kim et al. (2021) found that a single preoperative dose of intravenous ibuprofen reduced postoperative pain and opioid consumption for up to 24 hours. Zhou et al. (2023) also reported lower pain intensity and opioid use with intravenous ibuprofen in adult postoperative pain trials. Southworth et al. (2009) described reduced opioid requirements with intravenous ibuprofen after abdominal and orthopedic procedures. The current findings are consistent with these data and provide spine surgery specific evidence for a repeated multimodal schedule.

Combination therapy has been reported in other surgical populations. Lubis et al. (2021) found that paracetamol and ibuprofen reduced morphine requirement after total knee arthroplasty. Park et al. (2024) reported benefit after thyroidectomy. The present results support a mechanistic interpretation in which central paracetamol activity and peripheral NSAID activity provide additive analgesia.

The absence of monitored adverse effects is clinically relevant but should be interpreted with caution. Paracetamol safety depends on dose, hepatic risk and concurrent medicines. NSAID safety depends on renal, bleeding and gastrointestinal risk (McCrae et al., 2018). This study used short duration dosing and excluded patients with major contraindications, so the findings should not be generalized to higher risk populations without careful assessment.

The study had strengths, including random allocation, double blinding, a uniform anaesthetic technique, standardized PCA morphine dosing and predefined pain assessment intervals. Limitations included a single centre design, small sample size, a significant difference in duration of surgery and assessment limited to 24 hours. Longer recovery, chronic postsurgical pain, renal indices, liver enzymes and surgical bleeding were not evaluated. Acute postoperative pain can contribute to persistent pain states and future studies should include longer assessment and broader safety monitoring

(Ishida et al., 2022).

CONCLUSION

Combined intravenous ibuprofen 400 mg and intravenous paracetamol 1 g administered before induction and continued every 8 hours for 24 hours provided superior postoperative analgesia after spine surgery compared with either drug alone. The combination reduced 24 hour morphine consumption and intraoperative fentanyl use without observed PONV or monitored opioid related adverse effects. Larger multicentre trials with extended recovery assessment and formal safety monitoring are needed before broad protocol adoption.

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