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Comparison of the effects of Remifentanil, Paracetamol (Apotel), and Dexmedetomidine on postoperative pain management following abdominal hysterectomy

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Abstract

Background and Objective:Postoperative pain remains a significant clinical challenge, potentially triggering cardiovascular, respiratory, and endocrine complications. Adjuvant analgesics, including dexmedetomidine and remifentanil, are frequently utilized to optimize postoperative pain management. This study aimed to compare the analgesic efficacy of these agents following elective abdominal hysterectomy.Materials and Methods: This double-blind, randomized clinical trial enrolled 195 women scheduled for abdominal hysterectomy at Sina Ashtiani Hospital (Arak, Iran). Using block randomization, participants were allocated into three treatment groups: intravenous Paracetamol (Apotel), Dexmedetomidine, and Remifentanil. Postoperative pain intensity was assessed using the Visual Analog Scale (VAS) at predefined intervals. In addition, the duration of analgesia, total analgesic use, and hemodynamic indicators were recorded throughout the first 24 hours after surgery. Statistical tests were performed using SPSS software.Results: The total dose of analgesics used in the dexmedetomidine group was considerably less than the paracetamol group (P=0.041), with significantly longer duration of analgesia (P<0.0001). VAS scores after surgery were considerably lower in the dexmedetomidine group than in the other two groups (P<0.0001). Moreover, the mean arterial pressure (MAP) and heart rate were considerably lower, and arterial oxygen saturation (SpO2) was higher in the dexmedetomidine group than in the others (P<0.05).Conclusion: Dexmedetomidine is better than remifentanil and paracetamol (Apotel) in patients undergoing abdominal hysterectomy. It decreases postoperative analgesic demand and prolongs the duration of analgesia and gives a better hemodynamic profile, hence better management of blood pressure, heart rate, and oxygen saturation. Trial registration: Iranian Registry of Clinical Trials (IRCT), IRCT20191104045328N45. Registered on 9 October 2025 (prospectively registered).

1. Introduction

Hysterectomy is the most frequently performed major gynecological surgery and serves as the definitive treatment for a wide spectrum of pathologies. These encompass abnormal uterine bleeding, uterine fibroids, uterovaginal prolapse, endometriosis, adenomyosis, pelvic inflammatory disease, pelvic pain, gynecologic malignancies, and obstetric complications (1, 2). The United States continues to record the highest rates of this operation, with about 550,000 women receiving hysterectomy annually, with healthcare expenditures of more than 5 billion(3,4). According to the regional research in Iran, the prevalence of hysterectomy has been estimated to be around 10% in the northern regions of the nation (5). Significant differences in the incidence of hysterectomy have also been seen amongst Western countries where detailed epidemiological data are routinely gathered (6).

Postoperative pain is still one of the major concerns for surgical patients due to its substantial systemic effects, especially on the cardiovascular, respiratory, and endocrine systems (7). Optimizing analgesia with minimal medication-related side effects is crucial to facilitate postoperative recovery (8). Appropriate pain management has important physiological benefits and, conversely, insufficient control of postoperative pain can trigger a series of negative effects, including significant patient discomfort,

protracted immobilization, thromboembolic events, and pulmonary problems (9). The postoperative discomfort following abdominal hysterectomy is moderate to severe (10). It is widely believed that severe acute postoperative pain (11) occurs in 5%5% to 30%30% of patients receiving this treatment, and it is known to be a significant predictor factor for the development of chronic pain syndromes (12, 13). This discomfort usually reaches its maximal severity within the first 33 days after surgery (14). Traditional methods of therapy for postoperative pain are largely opioid based and are provided either systemically using patient-controlled analgesia (PCA) or neuraxially by epidural or spinal routes (15).

Research has shown that alpha-2 agonists, which were created for the treatment of hypertension and are used in the treatment of opioid withdrawal syndrome, are potent analgesics that may relieve opioid-induced hyperalgesia (16). Dexmedetomidine, an α2 adrenergic receptor agonist, has been widely studied and used as an adjunct in anesthetic and pain treatment protocols (17, 18). Dexmedetomidine is the most potent alpha-2 adrenergic receptor agonist currently available and was initially launched as a short-term intravenous sedation drug in intensive care settings (17). Although opioids are superior to dexmedetomidine regarding analgesic efficacy, the latter has been found to have a strong opioid-sparing effect, lowering opioid needs by 30% to 50% (18), and providing a safer sedative profile. This drug has been shown in several investigations to maintain hemodynamic stability without respiratory depression (19).

Paracetamol is a major inhibitor of cyclooxygenase enzymes, and its analgesic mechanism also involves interactions with the descending serotonergic system (20). It is an efficient analgesic and does not have the common adverse effects of the usual NSAIDs or opioids (21). Paracetamol is generally safe but has a well-documented risk of hepatotoxicity and is thought to account for nearly half of all acute liver failure cases in the United Kingdom and approximately 40% in the United States (22, 23). Intravenous paracetamol is an effective alternative for the treatment of mild-to-moderate postoperative pain and can be used alone or as a key component of a multimodal analgesic regimen (24).

Remifentanil is a very potent opioid agonist with ultra-fast onset and ultra-short duration of action. This unusual pharmacokinetic profile is due to the fast hydrolysis of its methyl ester bond by nonspecific blood and tissue esterases (25, 26). The context-sensitive half-time (time for 50% reduction in blood concentration after stopping infusion) is approximately 33 minutes and independent of the length of infusion (7). In an earlier trial, continuous infusion of remifentanil at a rate of 0.05 to 0.15 μg/kg/min demonstrated excellent postoperative analgesia following major procedures (27). Also, new data suggest that remifentanil is associated with a decreased incidence of side effects, especially postoperative nausea and vomiting (PONV), compared with fentanyl (28). Remifentanil exerts no significant detrimental effects on the cardiovascular system and lacks the cumulative properties typical of other opioids (7). Nevertheless, its intravenous administration can precipitate opioid-induced adverse events, most notably respiratory depression. To date, there is a paucity of studies evaluating the efficacy and adverse effect profile of remifentanil for postoperative pain management following abdominal surgery (7).

2. Materials and Methods

2.1. Study Design and Setting

This single-center, randomized, parallel-group, double-blind clinical trial was conducted at Sina Rezaei Ashtiani Hospital, Arak, Iran, among women scheduled to undergo elective abdominal hysterectomy. A total of 195 participants were allocated in a 1:1:1 ratio to three intervention groups receiving intravenous paracetamol (Apotel), dexmedetomidine, or remifentanil. The trial was prospectively registered in the Iranian Registry of Clinical Trials (IRCT) on 9 October 2025 (registration number: IRCT20191104045328N45). The present report was prepared in accordance with the CONSORT 2010 guidelines for randomized controlled trials.

2.2. Study Population, Sample Size, and Inclusion Criteria

The study population consisted of women aged 18–65 years who were scheduled to undergo elective abdominal hysterectomy at Sina Rezaei Ashtiani Hospital, Arak, Iran. A total of 195 eligible participants were enrolled and allocated equally to the three intervention groups, with 65 participants in each group. The target sample size of 195 participants was prespecified in the registered trial protocol.

Participants were eligible for inclusion if they were candidates for abdominal hysterectomy, were classified as American Society of Anesthesiologists (ASA) physical status I or II, and provided written informed consent before enrolment.

Patients were excluded if they had significant systemic diseases, including renal, hepatic, or cardiovascular disorders, hypertension, diabetes mellitus, or malignancy; a history of substance abuse or chronic analgesic use; known hypersensitivity to any of the study medications; or a history of seasonal allergy. Participants were also excluded from the final study procedures if they withdrew consent or if continuation in the trial was considered clinically inappropriate.

2.3. Randomization and Allocation Concealment

Participants were assigned to the three intervention groups according to a pre-generated block randomization sequence with a block size of six. The randomization sequence was generated using the Sealed Envelope randomization software before participant allocation. Eligible participants were enrolled consecutively and assigned according to the next allocation specified in the randomization sequence. The sequence was designed to ensure an unpredictable allocation pattern across the three study groups. Allocation concealment was maintained through the pre-generated randomization sequence so that the upcoming treatment assignment could not be predicted before participant allocation.

2.4.Blinding

The study was conducted using a double-blind design, in which both the participants and the outcome assessor were unaware of treatment allocation. Study medications were prepared in syringes labeled only with each participant’s medical record number, without any indication of their contents or assigned treatment group. The medications were administered by the attending anesthesiologist. Participants therefore remained unaware of the specific study medication they received. Outcome assessments were

performed by a designated assessor who recorded study outcomes using the participants' medical record numbers and remained blinded to both treatment allocation and the administered medication throughout data collection.

2.5. Data Collection and Outcome Measures

The study outcomes were prespecified in accordance with the registered trial protocol. The primary outcomes were postoperative pain intensity, duration of analgesia (pain relief period), and postoperative opioid consumption. Secondary outcomes included mean arterial pressure (MAP), heart rate (HR), and peripheral arterial oxygen saturation (SpO_2).

Postoperative pain intensity was assessed using the Visual Analog Scale (VAS). The VAS consisted of a 10-cm scale ranging from 0, indicating no pain, to 10, indicating the worst imaginable pain. Participants were asked to indicate the intensity of their pain on the scale, and the corresponding value was recorded as the pain score. Pain intensity was assessed in the recovery room and at 2, 4, 8, and 12 hours after surgery.

The duration of analgesia, defined as the postoperative pain-relief period, was evaluated during the first 24 hours after surgery through clinical follow-up and review of the patients' records. Total postoperative opioid consumption during the first 24 hours was also recorded from each participant's medical record.

Hemodynamic and respiratory variables were considered secondary outcomes. Mean arterial pressure was measured using non-invasive blood pressure monitoring, heart rate was recorded using continuous cardiac monitoring, and peripheral arterial oxygen saturation was measured by pulse oximetry. These parameters were recorded at the beginning of surgery and subsequently at 15-minute intervals until the end of surgery.

All outcome assessments were performed by the designated blinded outcome assessor, who was unaware of the participants' treatment allocation.

2.6. Study Interventions and Pharmacological Protocols

Participants were allocated to one of three intervention groups. All three groups received the same background medications, consisting of intravenous dexamethasone (16 mg), ondansetron (16 mg), and morphine (10 mg). The groups differed only with respect to the study analgesic administered.

Participants in the paracetamol group (Group A) received 1 g of intravenous paracetamol (Apotel) in addition to the standardized background medications. Participants in the dexmedetomidine group (Group B) received 30 µg of intravenous dexmedetomidine in addition to the same background medications. Participants in the remifentanil group (Group C) received 1 mg of intravenous remifentanil together with the standardized background medications.

All study medications were administered intravenously under the supervision of the attending anesthesiologist. No placebo group was included. To maintain participant blinding, study medication syringes were identified using the participants' medical record numbers without indicating the treatment allocation or syringe contents. Participants were therefore unaware of the specific study medication they received. Outcome assessment was subsequently performed by a blinded assessor, as described above.

2.7. Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD), as appropriate, and categorical variables were summarized using frequencies and percentages.

The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. For comparisons of continuous variables among the three study groups, one-way analysis of variance (ANOVA) was used for normally distributed data, whereas the Kruskal–Wallis test was applied to variables that did not meet the assumption of normality. Categorical variables were compared using the chi-square test.

For outcomes measured repeatedly over time, including pain intensity and hemodynamic parameters, repeated-measures analysis of variance within the general linear model framework was used to assess the effects of time, treatment group, and the time-by-group interaction. The Greenhouse–Geisser correction was applied to the repeated-measures analyses when appropriate. When an overall between-group difference was statistically significant, Tukey's post-hoc test was used for pairwise comparisons among the three treatment groups.

For postoperative opioid consumption and duration of analgesia, differences among the three intervention groups were evaluated using one-way ANOVA, followed by Tukey's post-hoc pairwise comparisons where a significant overall group effect was identified. All statistical tests were two-sided, and a P value <0.05 was considered statistically significant.

.2.8Ethics Approval and Consent to Participate

The study protocol was approved by the Research Ethics Committee of Arak University of Medical Sciences, Arak, Iran (Approval ID: IR.ARAKMU.REC.1404.048; approval date: 4 May 2025). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and applicable national regulations governing research involving human participants. Written informed consent to participate was obtained from all participants before enrolment. Participants were informed about the study procedures, confidentiality of their data, and their right to withdraw at any time without any effect on their medical care.

3. Results

A total of 195 women undergoing abdominal hysterectomy were included in the study and allocated equally to the three intervention groups, with 65 participants in each group. The mean age was 49.01 ± 4.30 years in the remifentanil group, 49.81 ± 4.77 years in the intravenous paracetamol (Apotel) group, and 49.93 ± 4.48 years in the dexmedetomidine group. There was no statistically significant difference in mean age among the three groups (P = 0.449). The flow of participants through the different phases of the trial, including enrolment, allocation, follow-up, and analysis, is presented in Figure 1.

3.1. Hemodynamic and Respiratory Parameters

The mean values of mean arterial pressure (MAP), heart rate (HR), and peripheral oxygen saturation (SpO_2) across the predefined measurement time points are presented in Table 1.

Table 1. Mean arterial pressure, heart rate, and peripheral oxygen saturation across the predefined measurement time points in the three study groups

Time point	Study group	MAP (mmHg), mean ± SD	HR (bpm), mean ± SD	SpO_2 (%), mean ± SD
	Remifentanil	82.21 ± 7.01	81.97 ± 3.46	97.81 ± 0.50
Baseline	Apotel	81.74 ± 7.47	81.26 ± 4.04	97.67 ± 1.12
	Dexmedetomidine	81.30 ± 6.96	81.69 ± 4.72	97.77 ± 0.39
	Remifentanil	79.21 ± 6.74	80.72 ± 4.43	98.08 ± 0.71
15 min	Apotel	79.34 ± 7.34	79.29 ± 4.73	98.12 ± 0.76
	Dexmedetomidine	76.61 ± 6.81	78.77 ± 5.03	98.34 ± 0.64
	Remifentanil	78.31 ± 6.08	80.73 ± 5.49	98.26 ± 0.92
30 min	Apotel	78.51 ± 6.78	80.18 ± 4.98	98.35 ± 0.87
	Dexmedetomidine	73.61 ± 6.17	76.87 ± 5.69	98.89 ± 0.83
	Remifentanil	79.35 ± 6.00	81.47 ± 5.27	98.20 ± 1.01
45 min	Apotel	79.60 ± 6.55	80.65 ± 4.97	98.32 ± 0.95
	Dexmedetomidine	72.37 ± 4.99	74.29 ± 6.22	99.06 ± 0.90
	Remifentanil	79.48 ± 6.26	81.80 ± 4.93	97.94 ± 0.93
60 min	Apotel	79.85 ± 6.71	81.29 ± 4.88	98.07 ± 0.91
	Dexmedetomidine	71.11 ± 4.61	73.26 ± 6.32	99.02 ± 0.86
	Remifentanil	79.67 ± 6.48	81.73 ± 4.41	97.77 ± 0.93
75 min	Apotel	79.78 ± 7.34	81.29 ± 4.89	98.12 ± 0.93
	Dexmedetomidine	70.40 ± 4.54	72.21 ± 6.20	98.80 ± 0.71
	Remifentanil	79.18 ± 6.38	81.73 ± 4.85	97.46 ± 0.90
Recovery	Apotel	79.55 ± 7.33	81.87 ± 5.33	98.04 ± 0.87
	Dexmedetomidine	70.00 ± 3.69	72.07 ± 6.83	98.54 ± 0.61
	Time	**P < 0.001**	**P < 0.001**	**P < 0.001**
Repeated-measures effect	**Group**	**P < 0.001**	**P < 0.001**	**P < 0.001**
	Time × group	**P < 0.001**	**P < 0.001**	**P < 0.001**

Repeated-measures analysis with Greenhouse–Geisser correction demonstrated significant effects of time, treatment group, and the time-by-group interaction for MAP, HR, and SpO_2 (all $P < 0.001$).

Tukey's post-hoc comparisons showed that the overall mean MAP was significantly lower in the dexmedetomidine group than in both the remifentanil and intravenous paracetamol groups (both $P < 0.001$), whereas no significant difference was observed between the remifentanil and paracetamol groups ($P = 0.989$).

Similarly, the overall mean HR was significantly lower in the dexmedetomidine group than in both other groups (both $P < 0.001$), while the difference between remifentanil and intravenous paracetamol was not statistically significant ($P = 0.660$).

For SpO_2, the dexmedetomidine group showed significantly higher overall values than the remifentanil and intravenous paracetamol groups (both $P < 0.001$). No significant difference was observed between the remifentanil and intravenous paracetamol groups ($P = 0.157$).

3.2. Postoperative Pain Intensity

Postoperative pain intensity was assessed using the Visual Analog Scale (VAS) in the recovery room and at 2, 4, 6, 12, and 24 hours after surgery (Table 2). These are the actual assessment time points reported in the study results.

Table 2. Visual Analog Scale pain scores in the recovery room and at 2, 4, 6, 12, and 24 hours after surgery in the three study groups

Time point	Study group	Mean VAS score	SD
	Remifentanil	0.74	0.99
Recovery	Apotel	0.72	0.96
	Dexmedetomidine	0.54	0.86
	Remifentanil	3.71	1.99
2 h after surgery	Apotel	3.29	2.02
	Dexmedetomidine	1.72	1.61
	Remifentanil	5.00	1.80
4 h after surgery	Apotel	5.32	1.80
	Dexmedetomidine	3.60	1.68
	Remifentanil	3.89	1.86
6 h after surgery	Apotel	4.21	1.83
	Dexmedetomidine	4.80	1.75
	Remifentanil	2.53	1.12
12 h after surgery	Apotel	2.83	1.29
	Dexmedetomidine	2.15	0.59
	Remifentanil	1.41	0.58
24 h after surgery	Apotel	1.52	0.59
	Dexmedetomidine	1.12	0.63

Repeated-measures ANOVA with Greenhouse–Geisser correction demonstrated significant effects of time, treatment group, and the time-by-group interaction on VAS pain scores (all $P < 0.001$).

Tukey's post-hoc analysis demonstrated that, overall across the repeated assessments, mean pain scores differed significantly between the dexmedetomidine group and both the remifentanil and intravenous paracetamol groups (both $P < 0.001$). No statistically significant overall difference was observed between the remifentanil and intravenous paracetamol groups ($P = 0.503$).

Although the dexmedetomidine group had lower mean VAS scores at recovery and at 2, 4, 12, and 24 hours after surgery, its mean VAS score at 6 hours was numerically higher than those observed in the remifentanil and intravenous paracetamol groups. Therefore, the treatment effect should be interpreted on the basis of the repeated-measures analysis rather than as superiority at every individual postoperative assessment.

3.3. Postoperative Opioid Consumption and Duration of Analgesia

The cumulative dose of postoperative opioid consumed during the first 24 hours was recorded in milligrams, whereas the duration of analgesia was recorded in hours.

Table 3. Postoperative opioid consumption during the first 24 hours and duration of analgesia among the three study groups

Variable	Study group	Mean	SD	Overall P value
	Remifentanil	56.92	17.40	
Opioid consumption (mg/24 h)	Apotel	57.69	18.18	0.048
	Dexmedetomidine	51.53	8.70	
	Remifentanil	3.17	1.36	
Duration of analgesia (h)	Apotel	3.25	1.21	<0.001
	Dexmedetomidine	4.40	1.53	

There was a statistically significant overall difference in postoperative opioid consumption among the three groups (P = 0.048). Tukey's post-hoc analysis showed that opioid consumption was significantly lower in the dexmedetomidine group than in the intravenous paracetamol group (P = 0.041). However, the difference between dexmedetomidine and remifentanil was not statistically significant (P = 0.116), nor was the difference between remifentanil and intravenous paracetamol (P = 0.956).

The duration of analgesia also differed significantly among the three groups (P < 0.001). The mean duration of analgesia was 4.40 ± 1.53 h in the dexmedetomidine group, compared with 3.17 ± 1.36 h in the remifentanil group and 3.25 ± 1.21 h in the intravenous paracetamol group. Post-hoc comparisons demonstrated significantly longer analgesia in the dexmedetomidine group than in both the remifentanil and intravenous paracetamol groups (both P < 0.001). No significant difference was observed between the remifentanil and intravenous paracetamol groups (P = 0.946).

4. Discussion

Abdominal hysterectomy remains one of the most frequently performed gynecological surgeries, notoriously associated with intense postoperative pain. If left inadequately managed, this pain can precipitate a cascade of respiratory and cardiovascular complications, ultimately prolonging hospital stays (29). While traditional opioids like morphine and fentanyl have long been the gold standard for analgesia, their well-known adverse effects, ranging from postoperative nausea to respiratory depression, have driven clinicians to explore alternative or opioid-sparing adjuncts. Therefore, drugs like remifentanil (ultra-short-acting opioid), intravenous paracetamol, and dexmedetomidine (very selective α2-adrenergic agonist) have been investigated in great detail because of their distinctive sedative and

analgesic characteristics (30). Despite a growing literature, no consensus yet exists on which of these medicines offers the best compromise between optimal pain control and minimization of side effects. This direct comparison between these three drugs in patients having a hysterectomy will give us solid evidence to fine-tune modern multimodal pain management regimens.

We found a substantial difference in the mean opioid use among the three intervention groups. In particular, post hoc analysis showed that patients who received dexmedetomidine needed much less rescue opioids than patients treated with IV paracetamol. Interestingly, the difference in opioid use between remifentanil and IV paracetamol groups and between remifentanil and dexmedetomidine cohorts were not statistically significant. This substantial decrease in the dexmedetomidine group is attributed to the powerful central analgesic characteristics of dexmedetomidine and its well-known opioid-sparing action. Dexmedetomidine acts as an agonist at α2-adrenergic receptors to attenuate nociceptive signal transmission at the spinal and supraspinal levels, hence reducing the overall requirement for supplementary opioids (31, 32). The findings are quite consistent with previous literature, which often shows a reduction of opioid dependency following the administration of dexmedetomidine, reinforcing its use as a valuable part of multimodal analgesic regimens. For example, Ji et al. showed that perioperative dexmedetomidine improves postoperative pain management and accelerates recovery pathways in patients after abdominal hysterectomy, thereby providing a valuable adjunct in surgical anesthesia (33).

Our results are in line with previous studies by Gurbet et al. (34) and Syed et al. (35), who both reported that dexmedetomidine, as an α2-adrenergic agonist, had a considerable opioid-sparing effect and greatly reduced the requirement of rescue analgesia after surgery. Mechanistically, this impact is due to its central action on the locus coeruleus and the dorsal horn of the spinal cord, where it suppresses the release of norepinephrine and Substance P, thus potentiating its overall antinociceptive profile (31). However, it is important to note that Landorf et al. saw a reduction in opioid requirements in the first 24 postoperative hours but did not see any meaningful effects on pain levels or PONV (36). However, our main findings are consistent with a broader literature of many meta-analyses, all concluding that perioperative dexmedetomidine substantially reduces postoperative pain and may potentially enhance neurocognitive outcomes (37).

A notable finding of our investigation was the longer duration of analgesia in the dexmedetomidine group (mean 4.40 hours), which was significantly longer than in both the remifentanil (3.17 hours) and IV paracetamol (3.25 hours) groups. This result is consistent with the results of Schnabel et al., who also found that dexmedetomidine successfully prolongs the duration of sensory blockage and delays the time for the first request for rescue medication (3838). The shorter duration of analgesia in our remifentanil group can be explained by its ultra-short half-life and the phenomena of opioid-induced hyperalgesia (OIH) which has been discussed at length by Lee et al. (39). In our research population (40), dexmedetomidine provided a more persistent and stable analgesic profile than IV paracetamol or remifentanil in the long term by increasing hemodynamic stability and synergizing with main anesthetic drugs.

The addition of dexmedetomidine to levobupivacaine in total abdominal hysterectomy blocks has also been found to improve postoperative analgesia and reduce the requirement of additional analgesics (9), which further supports our findings. Moreover, the equivalence between our remifentanil and IV paracetamol groups in terms of opioid consumption and duration of analgesia suggests that although the two regimens had different pharmacological mechanisms, their efficacy in postoperative pain control was comparable. Remifentanil is an ultra-short-acting opioid with a quick onset, which makes it ideal for intraoperative pain management, but it has little residual analgesic effect postoperatively owing to its exceptionally short half-life (41). Conversely, IV paracetamol, via inhibiting cerebral cyclooxygenase, is useful for mild-to-moderate pain, but as a single agent, it is generally insufficient to offer persistent analgesia in surgery associated with high-intensity pain (42). Indeed, previous investigations have shown that the simple replacement or mixing of these drugs without a more effective adjunct does not make a substantial difference in analgesic duration or opioid consumption (43). This is consistent with our findings and highlights the relative limitations of both medicines in providing long-term control of postoperative pain.

One of the main findings of this study was that the VAS pain scores in the dexmedetomidine group were significantly lower at all postoperative time points compared with the remifentanil and IV paracetamol groups. These results strongly suggest that dexmedetomidine is more effective in postoperative pain. This finding is very much in line with a large amount of previous work showing dexmedetomidine is typically superior to traditional opioids such as fentanyl and non-opioids such as IV paracetamol for postoperative pain management due to its combined sedative and analgesic effects. For example, in a trial of 60 women undergoing abdominal hysterectomy, co-administration of dexmedetomidine with bupivacaine significantly reduced post-operative pain and analgesic use compared with bupivacaine alone (44). Likewise, Ren et al. in a study of 90 candidates for hysterectomy found that addition of dexmedetomidine to sufentanil increased the analgesic effects and reduced side events without increasing the length of hospital stay (14). Elrefahy et al. also demonstrated that adjunct intraoperative infusion of dexmedetomidine during general anesthesia for major abdominal surgery improved postoperative pain control and reduced post-operative opioid doses (45). This profound analgesic effect is related to its mechanism of action on the neuroaxial pathways of somatic and visceral pain and is beneficial in the management of postoperative pain and increases the duration of pain relief, although there is a potential risk of bradycardia (45). Wang et al provide further evidence, showing that dexmedetomidine as an adjunct to local anesthesia in gallbladder surgery significantly reduced postoperative pain. The patients in the dexmedetomidine group had lower pain scores at the 4, 12, and 24-hour postoperative intervals than the controls (46).

The results of the present investigation showed that blood pressure was significantly reduced in patients in the dexmedetomidine group compared to the remifentanil and Apotel groups. This finding was consistent with the earlier studies, which reported a decreased intraoperative MAP with dexmedetomidine due to the suppression of norepinephrine release (47). Furthermore, dexmedetomidine has an improved ability to modulate hemodynamic responses and reduce plasma catecholamine levels compared to short-acting opioids (31,48). A meta-analysis published by Li et al. in

2021 found that dexmedetomidine improves intraoperative hemodynamic stability and decreases cardiovascular stress and postoperative adverse responses (49). In contrast, dexmedetomidine infusion was less successful than remifentanil in attaining controlled hypotension and optimizing surgical field visibility in the trial by Richa et al. (50). These effects are explained by α2-adrenergic agonist characteristics of dexmedetomidine and subsequent reduction in central sympathetic tone, offering more robust hemodynamic regulation compared to opioids (31).

Moreover, dexmedetomidine in the present study considerably decreased the heart rate compared with remifentanil and Apotel. This bradycardic action, consistent with the findings of Spafford et al., is mediated by central agonism of α2-adrenergic receptors. This mechanism is a good strategy to control heart rate, decreasing sympathetic tone and increasing vagal activity (51), a pathway previously discussed in a detailed review by Weerink et al. (2017)(52). Similarly, Jouybar et al. found that patients receiving dexmedetomidine had a lower, more regular HR than those getting remifentanil, but this was not in the bradycardic range (15). Furthermore, the arterial oxygen saturation rate in the dexmedetomidine group was considerably greater than in the remifentanil and Apotel groups. This finding corresponds with the well-established profile of dexmedetomidine in preserving respiratory function, suggesting that its pharmacological properties can more effectively enhance patients' respiratory status (53). During the surgical procedures, the α2-agonistic actions of dexmedetomidine reduce anxiety and improve breathing conditions (54). In this respect, dexmedetomidine was superior to remifentanil and fentanyl in providing postoperative hemodynamic and respiratory stability with similar pain control and patient consciousness in the post-anesthesia care unit (PACU) (55).

5. Conclusion

This study showed that dexmedetomidine reduced opioid consumption and prolonged the duration of analgesia. Dexmedetomidine was more effective than remifentanil and Apotel (intravenous acetaminophen) in preventing postoperative pain and required less rescue analgesic medication overall. In addition, as compared with the other two drugs, it had remarkably favorable effects on hemodynamic stability by significantly decreasing arterial blood pressure and heart rate, while simultaneously increasing arterial oxygen saturation. In general, dexmedetomidine is quite helpful for postoperative pain control and has a beneficial influence on vital signs such as blood pressure, heart rate, and oxygen saturation.

6. Limitations and Recommendations for Future Studies

The present study has some limitations, such as the sample size and the fact that only patients receiving abdominal hysterectomy were included. This limits the application of the findings to other surgical procedures. It is strongly advised that further studies with bigger sample sizes be conducted to confirm and improve the reliability of these findings. Furthermore, the long-term efficacy of dexmedetomidine should be assessed, and its side effects should be carefully assessed in follow-up periods longer than 24 h. Future research should also try to compare this medication with novel non-opioid analgesics, study different age groups and individuals with underlying comorbidities, and better explain the exact

mechanisms of action of dexmedetomidine. Studying its combined efficacy with various treatment approaches may potentially greatly improve the procedures for managing postsurgical pain.

Abbreviations

VAS: Visual Analog Scale; MAP: Mean Arterial Pressure; HR: Heart Rate; SpO_2: Peripheral Oxygen Saturation; IV: Intravenous; IRCT: Iranian Registry of Clinical Trials.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Research Ethics Committees of Arak University of Medical Sciences, Arak, Iran (Approval ID: IR.ARAKMU.REC.1404.048; approval date: 4 May 2025). The study was conducted in accordance with ethical principles and national standards for conducting medical research in Iran. Written informed consent to participate was obtained from all participants before enrolment.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

Not applicable**Funding**

Not applicable

Authors' contributions

Maryam Shokrpour, Alireza Kamali, Shirin Pazoki, Somayeh Nikfar: Conceptualization and Writing original draft.

Saba Safaei**:** Supervision, Conceptualization, Writing original draft and Writing review & editing.

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Not applicable

Trial registration

The trial was registered in the **Iranian Registry of Clinical Trials (IRCT)** under registration number **IRCT20191104045328N45** on **9 October 2025**.

Article type

Research Article.

Clinical trial number

IRCT20191104045328N45.

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Figures

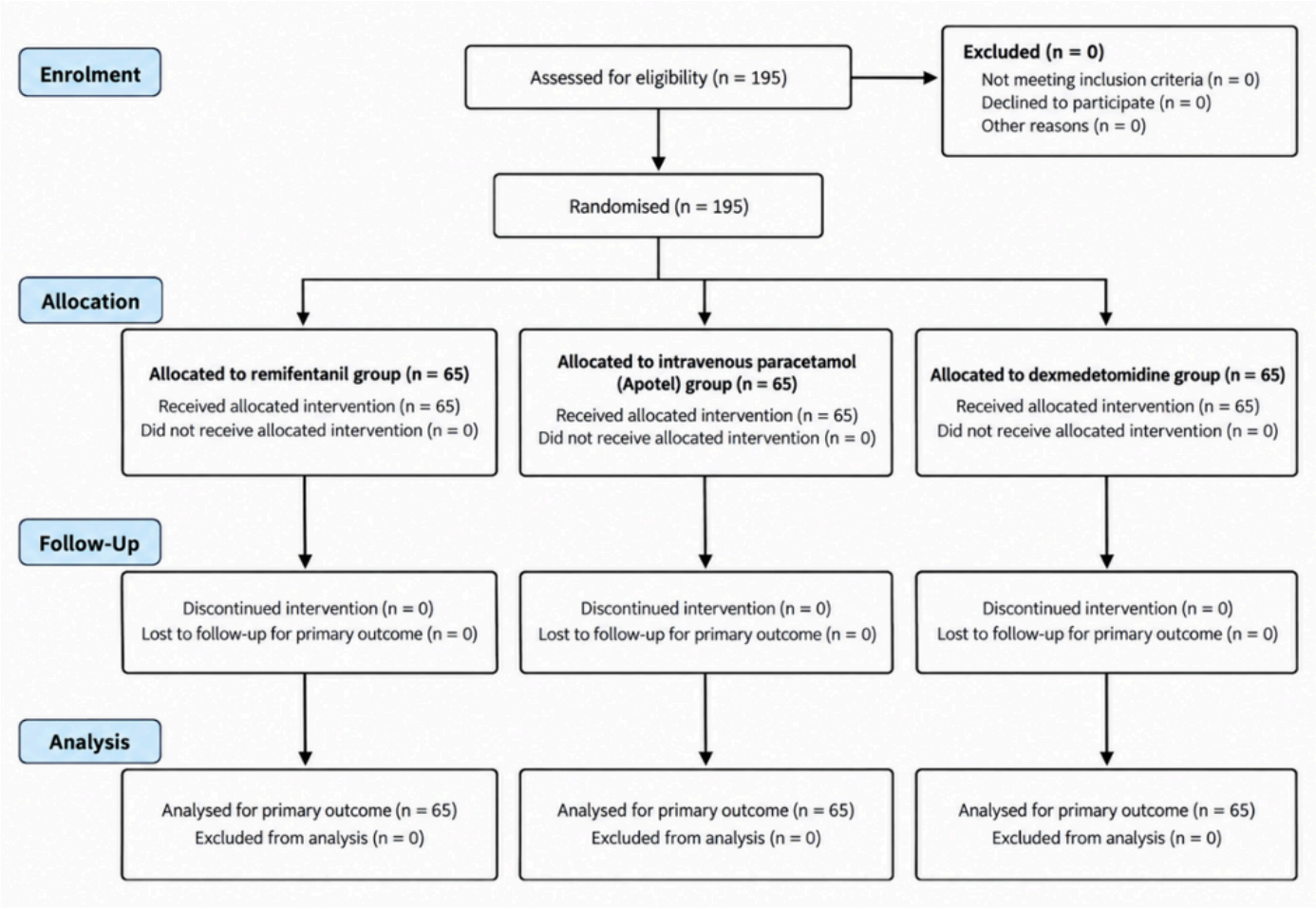


Figure 1

CONSORT 2025 flow diagram of participant enrolment, allocation, follow-up, and analysis in the three-arm randomised clinical trial.

Supplementary Files

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