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Effect of different doses of intravenous dexmedetomidine infusion combined with ropivacaine caudal block on acute and chronic pain after anorectal surgery

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Abstract: Objective To observe the effects of combining intravenous pump infusion of different doses of dexmedetomidine on acute and chronic pain, sedation, analgesic use, and adverse drug reactions in patients undergoing ropivacaine caudal block anesthesia for anorectal surgery. **Methods** A total of 96 patients scheduled for elective anorectal surgery in the Department of Anorectal Surgery, Xi'an Affiliated Hospital of Shaanxi University of Chinese Medicine from July 2021 to July 2023 were selected. According to a random number table method, patients were divided into Group A (n=32), Group B (n=32), and Group C (n=32). All three groups underwent ultrasound- guided caudal block anesthesia. Group A received an intravenous pump infusion of 50 mL of 0.9% sodium chloride injection. Group B received an intravenous pump infusion of dexmedetomidine 0.5 μg/kg (diluted to 50 mL with 0.9% sodium chloride injection). Group C received an intravenous pump infusion of dexmedetomidine 1 μg/kg (diluted to 50 mL with 0.9% sodium chloride injection). The mean arterial pressure (MAP), heart rate, sedation status, and pain status at different time points were compared among the three groups. The use of analgesic drugs and adverse drug reactions were recorded. A 6-month postoperative follow-up was conducted to record the incidence of chronic post- surgical pain (CPSP). **Results** The time effect, between-group effect, and interaction effect on intraoperative MAP and heart rate levels at different time points were statistically significant in all three groups (P<0.01). Pairwise comparisons showed that the fluctuations in MAP and heart rate levels in Group C were smaller than those in Group A and Group B, respectively (P<0.05). The time effect, between-group effect, and interaction effect on postoperative Visual Analogue Scale (VAS) scores at rest and during movement were statistically significant in all three groups (P<0.01). The VAS scores of Group C were lower than those of Group A and Group B, respectively (P<0.05). The time effect, between-group effect, and interaction effect on postoperative Ramsay Sedation Scale (RSS) scores were statistically significant in all three groups (P<0.01). Pairwise comparisons showed that the RSS scores of Group C were higher than those of Group A and Group B, respectively (P<0.05). There was a statistically significant difference in the time to first postoperative analgesic administration among the three groups (P<0.05); Group C was superior to Group B and Group A (P<0.05), and Group B was superior to Group A (P<0.05). There was a significant difference in the number of postoperative analgesic administrations among the three groups (Z=33.912, P<0.01). No significant difference was observed in the total incidence of adverse drug reactions among Group A, Group B, and Group C [31.25% (10/32) *vs* 18.75% (6/32) *vs* 31.25% (10/32), χ^2= 1.688, P=0.430]. There was a statistically significant difference in the incidence of CPSP at 6 months postoperatively among Group A, Group B, and Group C [19.35% (6/31) *vs* 3.13% (1/32) vs 0, χ^2=9.915, P=0.007]. Compared with Group A, Group C had a lower incidence of CPSP (P<0.05). **Conclusion** Compared with a low dose, a high dose of dexmedetomidine combined with ropivacaine caudal block can maintain stability in MAP and heart rate levels during anorectal surgery better, provide better postoperative sedation, have a significant effect on postoperative acute pain, prolong postoperative analgesia duration, and result in less CPSP.

Keywords: Dexmedetomidine; Ropivacaine; Caudal block; Chronic post-surgical pain; Sedation; Analgesics

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Anorectal diseases are common and frequently encountered clinical conditions, with surgical intervention being the primary treatment modality currently [1]. The perianal region is densely innervated with nerves and blood vessels, rendering the sensory nerves exceptionally sensitive. Postoperative pain often causes severe discomfort to patients, not only interfering with normal defecation function but also potentially leading to increased heart rate in elderly patients and raising the risk of cardiovascular and cerebrovascular complications [2-3]. The severity and duration of postoperative pain are closely associated with anesthesia techniques, anesthetic agents, and their dosages [4].

Caudal block anesthesia is widely used in anorectal surgeries due to its simplicity of operation, minimal invasiveness, and cost-effectiveness [5]. Ropivacaine, a commonly used amide-type local anesthetic, possesses the characteristic of differential sensory and motor nerve blockade. Compared to other agents in its class, ropivacaine exhibits lower toxicity to the cardiovascular and nervous systems [6-7]. However, when used alone, its analgesic duration is relatively short, and the analgesic

effect may not be comprehensive, often resulting in unsatisfactory postoperative pain relief.

Dexmedetomidine is a highly selective α2-adrenergic receptor agonist that can enhance the efficacy of local anesthetics in peripheral nerve blocks. It not only shortens the onset time of local anesthetics but also prolongs postoperative analgesia [8-10]. Currently, the combination of ropivacaine and dexmedetomidine has been applied in clinical surgical anesthesia. However, reports on the impact of dexmedetomidine choice in caudal block anesthesia on acute and chronic pain after anorectal surgery are relatively scarce [11]. Therefore, this study aims to investigate the effects of caudal block anesthesia with ropivacaine combined with different doses of dexmedetomidine on acute and chronic pain after anorectal surgery, providing a reference for formulating clinical anesthesia plans for anorectal surgeries.

1 Data and Methods

1.1 General Data

Ninety-six patients scheduled for elective anorectal surgery in the Department of Proctology at Xi'an Hospital of Traditional Chinese Medicine from July 2021 to July 2023 were selected.

Inclusion criteria: (1) Age ≥ 18 years and < 65 years; (2) American Society of Anesthesiologists (ASA) physical status classification I–II [12]; (3) First-time recipients of anorectal surgery; (4) Informed consent obtained from the patient or their family.

Exclusion criteria: (1) Presence of severe underlying diseases; (2) Suffering from immunodeficiency diseases; (3) Allergy to the drugs used in this study; (4) Women who are pregnant or lactating; (5) Suffering from psychiatric disorders; (6) Having neurovascular injuries; (7) Infection present in the caudal block area.

This study was approved by the Ethics Committee of Xi'an Hospital of Chinese Medicine (Ethics Approval No. LL0661).

Sample size calculation: Setting α=0.05, β=0.10, two-sided test, U_α=1.96, π=0.30, δ=0.1, the sample size per group $n = (U_\alpha)^2\pi(1-\pi)/\delta^2 = 80.67 \approx 81$. Considering a dropout rate of approximately 15%, the actual total sample size $N = 95.29 \approx 96$. Patients were divided into groups A, B, and C using a random number table, with 32 patients in each group. There were no statistically significant differences among groups A, B, and C in terms of age, gender composition, body mass index (BMI), ASA classification, caudal block time, and surgery time (P>0.05). **See Table 1.**

Tab.1 Comparison of general data among three groups ($\bar{x} \pm s$)

Group	Case	Age (years)	Gender (M/F, case)	BMI (kg/m²)	ASA		Sacral block time (min)	Surgery time (min)
					I	II		
Group A	32	44.27±12.35	17/15	22.71±2.24	16	16	6.69±1.73	32.86±15.21
Group B	32	45.36±12.94	13/19	23.17±2.03	18	14	6.81±1.88	32.79±15.34
Group C	32	44.61±11.89	15/17	23.36±2.18	19	13	6.77±1.76	33.41±16.07
***F*/χ^2 value**		0.043	1.004	0.509	0.590		0.025	0.010
***P* value**		0.988	0.605	0.677	0.745		0.995	0.999

1.2 Anesthesia Method

Three groups received the following treatment 15 minutes before sacral block:

Group A: Patients received an intravenous infusion of 50 mL of 0.9% sodium chloride injection.

Group B: Patients received an intravenous infusion of dexmedetomidine hydrochloride injection (Jiangsu Yangtze River Pharmaceutical Group, batch No.: H20183219, 2 mL: 0.2 mg) at 0.5 μg/kg, diluted to 50 mL with 0.9% sodium chloride injection.

Group C: Patients received an intravenous infusion of dexmedetomidine hydrochloride injection at 1 μg/kg, diluted to 50 mL with 0.9% sodium chloride injection.

Caudal block anesthesia: All patients underwent routine preoperative fasting. Upon entering the operating room, they were given oxygen via face mask, and vital signs were monitored. Prior to performing the caudal block, 400 mL of lactated Ringer's solution was preloaded via an intravenous cannula for volume expansion.

All patients were placed in the left lateral position for the caudal block. When in the lateral position, the back was arched posteriorly, knees drawn towards the abdomen, a small pillow placed under the hips, and legs slightly apart. The position of the coccyx tip was palpated first, followed by verification of the equilateral triangle structure formed by the apex of the sacral hiatus and the sacral cornua using color ultrasound.

After standard aseptic preparation and draping, a 22-gauge needle was used to penetrate the sacrococcygeal ligament and enter the sacral hiatus space. After confirming loss of resistance and absence of blood or cerebrospinal fluid upon aspiration, 20 mL of 0.5% ropivacaine hydrochloride injection (Shandong Ruiyang Pharmaceutical Co., Ltd., batch No.: H20183152, 10 mL: 100 mg) was slowly injected. Communication was maintained with the patient during drug injection, and patient responses were closely monitored.

The rescue analgesic for all patients postoperatively was parecoxib sodium 20 mg intravenously.

1.3 Observation Indicators

1.3.1 Hemodynamic Monitoring

Intraoperative mean arterial pressure (MAP) and heart rate were recorded for the three groups at the following time points: before anesthesia (T0), immediately after block (T1), 30 minutes after block (T2), and 1 hour postoperatively (T3). All assessments were performed by the same anesthesiologist (blinded).

1.3.2 Postoperative Sedation Assessment

Sedation levels in the three groups were assessed at 4 hours (T4), 12 hours (T5), 24 hours (T6), and 48 hours (T7) postoperatively using the Ramsay Sedation Scale (RSS) [13]. Patients were scored based on clinical state: 1 point: anxious, agitated, or restless; 2 points: cooperative, oriented, or tranquil; 3 points: asleep, responsive to commands; 4 points: asleep, responsive to light glabellar tap or loud auditory stimulus; 5 points: asleep, responsive only to noxious stimuli such as firm pressure; 6 points: asleep, unresponsive to any stimulus. A score of 1 indicated inadequate sedation, scores 2–4 indicated appropriate sedation, and scores 5 or 6 indicated oversedation. All assessments were performed by the same anesthesiologist (blinded).

1.3.3 Postoperative Pain Intensity Assessment (Primary Endpoint)

Visual Analogue Scale (VAS) score at rest and during movement [14]: VAS assessment at rest and during movement was performed for the three groups at T4, T5, T6, and T7. All assessments were performed by the same attending physician (blinded).

1.3.4 Analgesic Usage

The time to first rescue analgesic request postoperatively and the number of patients requiring rescue analgesics, as well as the frequency of rescue analgesic use within 24 hours, were recorded for the three groups. All assessments were performed by the same attending physician (blinded).

1.3.5 Adverse Drug Reactions

The occurrence of adverse reactions such as nausea/vomiting, bradycardia, pruritus, hypotension, and excessive sedation was recorded for the three groups. All assessments were performed by the same attending physician (blinded).

1.3.6 Assessment of Chronic Post-Surgical Pain (CPSP) (Secondary Endpoint)

Follow-up via hospital review or telephone was conducted to record the incidence of CPSP at 6 months postoperatively in the three groups.Criteria for CPSP: New-onset pain in or near the surgical area persisting for more than 1 week at 6 months postoperatively, with a VAS score > 3, was diagnosed as CPSP. All assessments were performed by the same attending physician (blinded).

1.4 Statistical Methods

Data analysis was performed using SPSS 26.0 statistical software. Normally distributed measurement data are expressed as $\bar{x} \pm s$. Intergroup comparisons were performed using one-way ANOVA. Comparisons across different time points were performed using repeated measures ANOVA, with pairwise comparisons conducted using the LSD-t test. Count data are expressed as number (percentage) and compared using the chi-square test. The frequency of rescue analgesic use among the three groups was compared using the Kruskal-Wallis H test, with pairwise comparisons conducted using the Mann-Whitney U test. A P value < 0.05 was considered statistically significant.

2 Results

2.1 Comparison of Intraoperative Hemodynamic Changes Among Three Groups

For mean arterial pressure (MAP) and heart rate (HR) levels at different intraoperative time points, the time effect, group effect, and group-by-time interaction effect were all statistically significant (P<0.01). Pairwise comparisons revealed that Group C exhibited smaller fluctuations in MAP and HR levels. **See Table 2.**

2.2 Comparison of Postoperative VAS Scores at Resting and Motion Among Three Groups

For VAS scores at resting and motion at different postoperative time points, the time effect, group effect, and group-by-time interaction effect were all statistically significant (P<0.01). Pairwise comparisons showed that VAS scores were lower in Group C (P<0.05). See **Table 3**.

Tab.2 Comparison of MAP and heart rate at different time points during surgery in three groups (n=32, $\bar{x}\pm s$)

Group	MAP (mmHg)				HR (times/min)			
	T0	T1	T2	T3	T0	T1	T2	T3
Group A	78.35±7.63	86.26±7.48[a]	76.16±7.02[b]	78.40±6.82[b]	65.82±6.74	70.58±7.02[a]	76.47±6.81[ab]	70.38±6.25[ac]
Group B	79.76±7.71	83.51±6.89[a]	77.42±6.83[bd]	78.46±6.51[b]	65.79±6.81	68.39±6.97	71.33±6.50[ad]	69.19±7.06
Group C	78.41±7.60	82.68±6.92[a]	76.50±7.13[bd]	77.53±6.95[b]	66.05±6.78	68.13±7.12	70.69±6.91[ad]	67.37±7.14
$F_{\text{time/ group/interaction}}$ **value**	15.449/23.610/19.824				18.353/26.571/34.643			
$P_{\text{time/ group/interaction}}$ **value**	<0.001/<0.001/<0.001				<0.001/<0.001/<0.001			

Note: Compared with T0,[a]P<0.05; Compared with T1,[b]P<0.05; Compared with T2, [c]P<0.05;Compared with Group A, [d]P<0.05.

Tab.3 Comparison of VAS scores between three groups of postoperative resting motion at different times (n=32, point, $\bar{x}\pm s$)

Group	Resting				Motion			
	T4	T5	T6	T7	T4	T5	T6	T7
Group A	2.84±1.94	2.53±1.89	2.33±1.80	1.75±1.72[a]	3.26±2.01	3.45±1.84	3.28±1.81	2.89±1.65
Group B	2.31±1.67	1.83±1.36	1.38±1.27[ad]	1.26±1.06[a]	2.63±1.66	2.92±1.57	2.67±1.54	2.15±1.33[b]
Group C	1.85±1.53[d]	1.80±1.50	1.36±1.25[d]	0.95±0.71[abd]	2.61±1.64	2.89±1.59	2.43±1.51[d]	1.74±1.21[abcd]
$F_{\text{time/ group/interaction}}$ **value**	23.725/30.261/35.814				17.594/28.823/34.201			
$P_{\text{time/ group/interaction}}$ **value**	<0.001/<0.001/<0.001				<0.001/<0.001/<0.001			

Note: Compared with T4, [a]P<0.05; Compared with T5, [b]P<0.05; Compared with T6, [c]P<0.05; Compared with Group A, [d]P<0.05.

2.3 Comparison of Postoperative RSS Scores Among Three Groups

For postoperative Ramsay Sedation Scale (RSS) scores, the time effect, group effect, and group-by-time interaction effect were all statistically significant (P<0.01). Pairwise comparisons indicated that RSS scores were higher in Group C (P<0.05). See **Table 4**.

2.4 Comparison of Postoperative Analgesic Use Among Three Groups

There was a statistically significant difference in the time to first rescue analgesia among the three groups (F = 178.640, P<0.01). Compared to Group A, the time to first rescue analgesia was longer in Group B and Group C (P<0.05); furthermore, the time was significantly longer in Group C than in Group B (P<0.05).The difference in the frequency of rescue analgesia among the three groups was also statistically significant (P<0.01). The frequency in Group A was higher than those in Group B and Group C (Z=3.992, P<0.01; Z=5.468, P<0.01), while no significant difference was observed between Group C and Group B (Z=1.834, P=0.067). See **Table 5**.

2.5 Adverse Drug Reactions Among Three Groups

There was no statistically significant difference in the overall incidence of adverse drug reactions among Groups A, B, and C (χ^2=1.688, P=0.430). See **Table 6**.

2.6 Occurrence of CPSP Among Three Groups

In Group A, one patient was lost to follow-up and excluded, leaving 31 cases; no patients were lost to follow-up in Groups B or C. At 6 months postoperatively, the incidence of CPSP in Groups A, B, and C was 19.35% (6/31), 3.13% (1/32), and 0, respectively, with a statistically significant difference among the three groups (χ^2=9.915, P=0.007). Compared to Group A, the incidence of CPSP was lower in Group C (P<0.05); however, no statistically significant difference was found between Group B and Group C (P>0.05).

Tab.4 Comparison of Ramsay sedation scores among three groups after surgery (n=32, point, $\bar{x}\pm s$)

Group	T4	T5	T6	T7
Group A	1.53±0.42	1.82±0.36[a]	2.03±0.40[ab]	2.33±0.36[abc]
Group B	2.24±0.36[d]	2.48±0.45[ad]	2.36±0.42[d]	2.39±0.35
Group C	2.46±0.38[de]	2.69±0.41[ade]	2.58±0.43[de]	2.38±0.37
$F_{\text{time/ group/ interaction}}$ value	28.716/39.641/37.594			
$P_{\text{time/ group/ interaction}}$ value	<0.001/<0.001/<0.001			

Note: Compared with T4, [a]P<0.05; Compared with T5, [b]P<0.05; Compared with T6, [c]P<0.05; Compared with Group A, [d]P<0.05; Compared with Group B, [e]P<0.05.

Tab.5 Use of postoperative analgesics in three groups (n=32)

Group	Time of first postoperative analgesic addition (min, $\bar{x}\pm s$)	Number of additional analgesics (case)		
		0	1 time	2 times
Group A	348.21±74.30	6	21	5
Group B	608.62±69.19[a]	22	9	1
Group C	820.48±90.04[ab]	28	4	0
F/H value	178.640	33.912		
P value	<0.001	<0.001		

Note: Compared with Group A, [a]P<0.05; Compared with Group B, [b]P<0.05.

Tab.6 Comparison of adverse reactions of three groups of drugs[n=32,case(%)]

Group	Nausea and vomiting	Bradycardia	Itchy Skin	Hypotension	Excessive Sedation	Total Incidence Rate (%)
Group A	7(21.88)	1(3.13)	1(3.13)	1(3.13)	0	31.25
Group B	3(9.38)	2(6.25)	0	0	1(3.13)	18.75
Group C	5(15.63)	2(6.25)	1(3.13)	0	2(6.25)	31.25
χ^2 value						1.688
P value						0.430

3 Discussion

Postoperative pain is a common complication following anorectal surgery. Its occurrence is primarily related to surgical trauma, inflammatory responses at the wound site, and spasms of the anal sphincter [15-16]. The choice of anesthetic agents is crucial for the clinical management of both acute and chronic postoperative pain. Ropivacaine, as a new long-acting amide local anesthetic, has become the preferred local anesthetic for caudal block anesthesia due to its minimal impact on the circulatory and respiratory systems and its lower risk of toxic reactions [17-18]. Since caudal block typically involves a single injection, its duration of action is relatively short, often necessitating combination with other drugs to prolong the effect. Dexmedetomidine belongs to the imidazole class of compounds and possesses multiple pharmacological effects, including sedation, analgesia, maintenance of hemodynamic stability, and attenuation of stress responses [19-20]. Relevant studies indicate that dexmedetomidine exhibits a synergistic analgesic effect with ropivacaine, potentially reducing the required dosage of ropivacaine [21-22]. However, whether the chosen dose of dexmedetomidine influences postoperative pain requires further investigation. This study analyzed the effects of caudal block anesthesia with ropivacaine combined with different doses of dexmedetomidine on acute and chronic pain after anorectal surgery.

The results of this study showed that compared to Group A, Group B and Group C exhibited smaller fluctuations in hemodynamic parameters before and after surgery. Furthermore, compared to Group A, the RSS scores at T4, T5, and T6 were higher in Group B and Group C. This indicates that dexmedetomidine can help maintain hemodynamic stability and provides good sedative effects following anorectal surgery under caudal block anesthesia. The reason for this is that when dexmedetomidine initially enters the bloodstream, its concentration is relatively high.

It acts on α2-adrenergic receptors on vascular smooth muscle, causing vasoconstriction and a consequent rise in blood pressure. As the drug's effect continues, α2-adrenergic receptors in the medullary center are activated, reducing the release of norepinephrine within the central nervous system, thereby lowering sympathetic nerve activity, leading to decreased blood pressure and heart rate. This finding aligns with the research results of Zheng *et al.* [23]. Additionally, dexmedetomidine activates α2 receptors in the locus coeruleus of the brainstem, promotes the expression of γ-aminobutyric acid (GABA) receptors in the central nervous system, and facilitates the hyperpolarization of noradrenergic neurons, effectively achieving its sedative effect [24]. Comparative analysis revealed that the sedation scores in Group C were significantly higher than those in Group B, suggesting that appropriately increasing the dose of dexmedetomidine can enhance the sedative effect.

This study analyzed changes in postoperative VAS scores at rest and during movement. The results suggest that the combination of dexmedetomidine and ropivacaine can effectively alleviate patients' acute postoperative pain. It was also found that this combination can prolong the duration of analgesia and reduce the need for postoperative rescue analgesics, with a higher dose of dexmedetomidine providing better analgesic efficacy. The reason for this is analyzed as follows: Dexmedetomidine binds to presynaptic α2 receptors on neurons in the dorsal horn of the spinal cord, inhibiting the release of norepinephrine. Simultaneously, it activates postsynaptic α2 receptor-mediated G-proteins, opening potassium ion influx channels. Both actions promote cellular hyperpolarization, thereby blocking the transmission of pain signals [25-26]. A higher dose of dexmedetomidine can more fully occupy these receptors, thereby strengthening the inhibition of pain signals. On the other hand, dexmedetomidine may also exert analgesic effects through peripheral mechanisms by inhibiting hyperexcitability of peripheral neurons and reducing the release of inflammatory mediators. Particularly at higher doses, dexmedetomidine may have stronger anti-inflammatory and analgesic effects in the peripheral nervous system, further extending the duration of postoperative analgesia [27].

Furthermore, in this study, the incidence of CPSP at 6 months postoperatively was lower in Group B and Group C compared to Group A, indicating that dexmedetomidine may help reduce the occurrence of chronic pain after anorectal surgery. This is likely because preemptive analgesia can attenuate the intensity of painful stimuli to peripheral nociceptors, thereby reducing the sensitivity of both peripheral and central nervous systems. However, this study is limited by its relatively small sample size and short follow-up duration. Future research should expand the sample size and extend the follow-up period to further investigate the role of dexmedetomidine in managing chronic pain after anorectal surgery.

The results of this study also showed that the incidence of excessive sedation in Group C was slightly higher than in the other two groups. This is related to the fact that at higher concentrations, dexmedetomidine enhances its agonistic effect on α2-adrenergic receptors, excessively inhibiting the release of norepinephrine. This mechanism leads to a significant reduction in sympathetic nervous system excitability, shifting the dynamic balance between wakefulness and sleep towards deeper sedation. This suggests that in the anesthetic management of anorectal surgery, clinicians must fully consider the relationship between analgesic needs and sedation risks. Developing individualized dosing regimens and implementing continuous dynamic monitoring can help achieve an optimal balance between sedation depth and safety. Additionally, there was no statistically significant difference in the overall incidence of adverse reactions among the three groups. This result indicates that caudal block anesthesia with dexmedetomidine combined with ropivacaine has a favorable safety profile in the treatment plan for patients with postoperative pain after anorectal surgery.

In summary, caudal block anesthesia with dexmedetomidine combined with ropivacaine demonstrates significant efficacy in patients after anorectal surgery. It not only helps maintain hemodynamic stability but also exhibits good sedative effects. It is particularly effective against acute postoperative pain, reduces the frequency of postoperative rescue analgesic use, and shows a high safety profile. Within this combination, a higher dose of dexmedetomidine appears to offer superior effects.

Conflict of Interest None

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·论 著·

静脉泵注不同剂量右美托咪定联合罗哌卡因骶管阻滞对肛肠术后急慢性疼痛的影响

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摘要：目的 观察在肛肠手术罗哌卡因骶管阻滞麻醉中，联合静脉泵注不同剂量右美托咪定对患者急慢性疼痛、镇静、镇痛药使用情况及药物不良反应的影响。**方法** 选择2021年7月至2023年7月陕西中医药大学西安附属医院肛肠科收治的择期行肛肠手术的患者96例，按照随机数字表法将患者分为A组（n=32）、B组（n=32）和C组（n=32）。三组均在超声引导下行骶管阻滞麻醉，A组静脉泵注0.9%氯化钠注射液50 mL；B组给予静脉泵注右美托咪定0.5 μg/kg（使用0.9%氯化钠注射液稀释至50 mL）；C组给予静脉泵注右美托咪定1 μg/kg（使用0.9%氯化钠注射液稀释至50 mL）。比较三组患者不同时间平均动脉压（MAP）、心率、镇静情况及疼痛情况，统计患者镇痛药使用情况及药物不良反应，术后6个月随访，统计慢性术后疼痛（CPSP）发生情况。**结果** 三组术中的MAP和心率的时间效应、组间效应及交互效应，均有统计学意义（P<0.01）；两两比较，C组MAP、心率水平波动分别小于A组和B组（P<0.05）。三组术后静息状态、运动状态视觉模拟评分（VAS评分）时间效应、组间效应及交互效应，均有统计学意义（P<0.01）；C组VAS评分分别低于A组和B组（P<0.05）。三组术后Ramsay镇静量表（RSS）评分时间效应、组间效应及交互效应，均有统计学意义（P<0.01）；两两比较，C组RSS评分分别高于A组和B组（P<0.05）。三组术后首次追加镇痛药时间的比较，差异有统计学意义（P<0.05）；且C组优于B组和A组（P<0.05），B组优于A组（P<0.05）。三组追加镇痛药次数差异有统计学意义（Z=33.912，P<0.01）。A组、B组和C组药物不良反应总发生率比较差异无统计学意义[31.25%（10/32）*vs* 18.75%（6/32）*vs* 31.25%（10/32），χ^2=1.688，P=0.430]。A组、B组和C组术后6个月的CPSP发生率差异具有统计学意义[19.35%（6/31）*vs* 3.13%（1/32）*vs* 0，χ^2=9.915，P=0.007]；与A组相比，C组的CPSP发生率较低（P<0.05）。**结论** 与低剂量相比，高剂量右美托咪定联合罗哌卡因骶管阻滞麻醉更能维持肛肠手术患者术中MAP和心率水平的稳定，术后镇静效果更好，对术后急性疼痛效果显著，能够延长术后镇痛时间，CPSP发生少。

关键词： 右美托咪定；罗哌卡因；骶管阻滞；慢性术后疼痛；镇静；镇痛药
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Effect of different doses of intravenous dexmedetomidine infusion combined with ropivacaine caudal block on acute and chronic pain after anorectal surgery

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Abstract: Objective To observe the effects of combining intravenous pump infusion of different doses of dexmedetomidine on acute and chronic pain, sedation, analgesic use, and adverse drug reactions in patients undergoing ropivacaine caudal block anesthesia for anorectal surgery. **Methods** A total of 96 patients scheduled for elective anorectal surgery in the Department of Anorectal Surgery, Xi'an Affiliated Hospital of Shaanxi University of

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Chinese Medicine from July 2021 to July 2023 were selected. According to a random number table method, patients were divided into Group A (n=32), Group B (n=32), and Group C (n=32). All three groups underwent ultrasound-guided caudal block anesthesia. Group A received an intravenous pump infusion of 50 mL of 0.9% sodium chloride injection. Group B received an intravenous pump infusion of dexmedetomidine 0.5 μg/kg (diluted to 50 mL with 0.9% sodium chloride injection). Group C received an intravenous pump infusion of dexmedetomidine 1 μg/kg (diluted to 50 mL with 0.9% sodium chloride injection). The mean arterial pressure (MAP), heart rate, sedation status, and pain status at different time points were compared among the three groups. The use of analgesic drugs and adverse drug reactions were recorded. A 6-month postoperative follow-up was conducted to record the incidence of chronic post-surgical pain (CPSP). **Results** The time effect, between-group effect, and interaction effect on intraoperative MAP and heart rate levels at different time points were statistically significant in all three groups (P<0.01). Pairwise comparisons showed that the fluctuations in MAP and heart rate levels in Group C were smaller than those in Group A and Group B, respectively (P<0.05). The time effect, between-group effect, and interaction effect on postoperative Visual Analogue Scale (VAS) scores at rest and during movement were statistically significant in all three groups (P<0.01). The VAS scores of Group C were lower than those of Group A and Group B, respectively (P<0.05). The time effect, between-group effect, and interaction effect on postoperative Ramsay Sedation Scale (RSS) scores were statistically significant in all three groups (P<0.01). Pairwise comparisons showed that the RSS scores of Group C were higher than those of Group A and Group B, respectively (P<0.05). There was a statistically significant difference in the time to first postoperative analgesic administration among the three groups (P<0.05); Group C was superior to Group B and Group A (P<0.05), and Group B was superior to Group A (P<0.05). There was a significant difference in the number of postoperative analgesic administrations among the three groups (Z=33.912, P<0.01). No significant difference was observed in the total incidence of adverse drug reactions among Group A, Group B, and Group C [31.25%(10/32) *vs* 18.75%(6/32) *vs* 31.25%(10/32), χ^2=1.688, P=0.430]. There was a statistically significant difference in the incidence of CPSP at 6 months postoperatively among Group A, Group B, and Group C [19.35%(6/31) *vs* 3.13%(1/32) *vs* 0, χ^2=9.915, P=0.007]. Compared with Group A, Group C had a lower incidence of CPSP (P<0.05). **Conclusion** Compared with a low dose, a high dose of dexmedetomidine combined with ropivacaine caudal block can maintain stability in MAP and heart rate levels during anorectal surgery better, provide better postoperative sedation, have a significant effect on postoperative acute pain, prolong postoperative analgesia duration, and result in less CPSP.

Keywords: Dexmedetomidine; Ropivacaine; Caudal block; Chronic post-surgical pain; Sedation; Analgesics

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肛肠疾病是临床中常见且多发的病症，当前主要治疗手段为手术治疗[1]。肛周神经血管密集，感觉神经异常敏锐，术后疼痛常给患者造成剧烈不适，不仅干扰患者的正常排便功能，还可能引发老年患者心率加快并增加心脑血管并发症的风险[2-3]。术后疼痛的程度及其持续时间与麻醉技术、麻醉药物及其剂量密切相关[4]。骶管阻滞麻醉在肛肠科手术中应用广泛，具有操作简便、创伤轻微及经济实用的优势[5]。罗哌卡因作为常用的酰胺类局部麻醉药物，具备感觉与运动神经阻滞分离的特性，相较于其他同类药物，罗哌卡因对心血管系统及神经系统的毒性更低[6-7]。然而，单独使用罗哌卡因时，其镇痛维持时间相对较短，且镇痛效果可能不够全面，以致术后镇痛效果往往不尽人意。右美托咪定是一种高度选择性的α2肾上腺素受体激动剂，能够增强局部麻醉药物对周围神经阻滞的效能，不仅能缩短局部麻醉药的起效时长，还能延长术后镇痛效果[8-10]。目前临床上已将罗哌卡因联合右美托咪定应用于外科手术麻醉中，但关于骶管阻滞麻醉中右美托咪定的选择对肛肠术后急慢性疼痛的影响，相关报道较为稀缺[11]。故本研究旨在探究不同剂量下右美托咪定联合罗哌卡因骶管阻滞麻醉对肛肠术后急慢性疼痛的影响，为临床肛肠手术麻醉方案的制定提供参考依据。

1 资料与方法

1.1 一般资料 选取2021年7月至2023年7月在西安市中医医院肛肠科择期行肛肠手术的96例患者。纳入标准：（1）年龄≥18岁，且<65岁；（2）美国麻醉医师协会（American Society of Amesthesiologists，ASA）分级为Ⅰ~Ⅱ级[12]；（3）首次接受肛肠手术；（4）患者或家属对本研究知情同意。排除标准：

（1）合并严重基础疾病；（2）患有免疫缺陷性疾病；（3）对本研究使用药物过敏；（4）正处于妊娠阶段或哺乳期间的女性；（5）患有精神类疾病；（6）患有神经血管损伤；（7）骶管阻滞区域存在感染。本研究已获得西安市中医医院伦理委员会审查通过（伦理批件号为LL0661）。

样本量估算：设α=0.05，β=0.10，双侧检验，U_α=1.96，π=0.30，δ=0.1，每组样本数$n=(U_\alpha)^2\pi(1-\pi)/\delta^2$=80.67≈81，考虑到15%左右的脱落率，实际总样本量为N=95.29≈96。按照随机数字表法将患者分为A、B、C组，各32例。A组、B组和C组患者年龄、性别构成、身体质量指数（body mass index，BMI）、ASA分级、骶管阻滞时间和手术时间的比较，差异均无统计学意义（P>0.05）。见表1。

1.2 麻醉方法 在骶管阻滞前15 min：A组患者接受静脉泵注0.9%氯化钠注射液50 mL；B组接受静脉泵注盐酸右美托咪定注射液（江苏扬子江药业，批号：H20183219，2 mL∶0.2 mg）0.5 μg/kg，使用0.9%氯化钠注射液稀释至50 mL；C组接受静脉泵注盐酸右美托咪定注射液1 μg/kg，使用0.9%氯化钠注射液稀释至50 mL。骶管阻滞麻醉：所有患者常规术前禁食，入室后给予面罩吸氧、心电监护监测生命体征。在实施骶管阻滞前，通过静脉留置针预先给予400 mL乳酸钠林格注射液进行扩容。所有患者取左侧卧位进行骶管阻滞，侧卧位时腰背向后弓曲，两膝向腹部靠拢，在髋部垫一小枕，两腿略分开，穿刺前先摸清尾骨尖端位置，随后通过彩色超声验证骶裂孔顶端与骶角形成的等边三角形结构。经过标准的无菌消毒与铺巾准备后，采用22号针头穿透骶尾韧带并进入骶裂孔间隙，确定无阻力且回抽无血液或脑脊液后，缓慢注入0.5%盐酸罗哌卡因注射液（山东瑞阳制药，批号：H20183152，10 mL∶100 mg）20 mL，在药物注射过程中保持与患者交流，密切观察患者反应。所有患者术后追加镇痛药均为帕瑞昔布钠20 mg静脉注射。

1.3 观察指标

1.3.1 血流动力学监测 术中记录3组患者麻醉前（T0）、阻滞后即刻（T1）、阻滞后30 min（T2）、术后1 h（T3）的平均动脉压（mean arterial pressure，MAP）及心率。所有患者均由同一位麻醉医师（采用盲法）进行评估。

1.3.2 术后镇静情况评估 三组分别在术后4 h（T4）、12 h（T5）、24 h（T6）、48 h（T7）采用Ramsay镇静量表（Ramsay Sedation Scale，RSS）评估[13]。根据患者临床状态打分，1分：患者焦虑、激动或者不安；2分：患者是合作、服从或者安静状态；3分：患者入睡，对命令有反应；4分：患者入睡，对轻度摇晃或大声音刺激有反应；5分：患者入睡，对伤害性刺激，如用力压迫有反应；6分：指患者入睡，对上述刺激无任何反应。其中1分表示镇静不足，2~4分表示镇静恰当，5分或6分表示患者镇静过度。所有患者均由同一位麻醉医师（采用盲法）进行评估。

1.3.3 术后疼痛程度评估（主要终点） 静息和运动状态下视觉模拟疼痛评分（Visual Analogue Scale，VAS）[14]：三组分别在T4、T5、T6、T7进行静息和活动状态下行VAS评估。所有患者均由同一位主治医师（采用盲法）进行评估。

1.3.4 镇痛药使用情况 记录三组患者术后第1次追加镇痛药的时间及24 h内追加镇痛药的例数、次数。所有患者均由同一位主治医师（采用盲法）进行评估。

1.3.5 药物不良反应 记录三组恶心呕吐、心动过缓、皮肤瘙痒、低血压、过度镇静等不良反应的发生情况。所有患者均由同一位主治医师（采用盲法）进行评估。

1.3.6 慢性术后疼痛（chronic post-surgical pain，CPSP）的评估（次要终点） 采用到院复查及电话随访的方式，记录三组患者术后6个月CPSP的发生情况。CPSP判定标准：术后6个月手术或手术相近区域有新发疼痛，疼痛持续超过1周，且VAS>3分诊断为CPSP。所有患者均由同一位主治医师（采用盲法）进行评估。

1.4 统计学方法 数据分析采用SPSS 26.0统计软件。符合正态分布的计量资料以$\bar{x}\pm s$表示，组间比较采用单因素分析，不同时间点比较采用重复测量方差分析，两两比较采用LSD-t检验。计数资料以例（%）表示，比较采用χ^2检验。追加镇痛药次数三组比较采用Kruskal-Wallis H检验，两两比较采用Mann-Whitney U检验。P<0.05为差异有统计学意义。

2 结 果

2.1 三组术中血流动力学变化比较 三组术中不同时间点MAP水平时间效应、组间效应及组间×时间交互效应，均有统计学意义（P<0.01）；三组术中不同时间点心率水平时间效应、组间效应及组间×时间交互效应，均有统计学意义（P<0.01）。两两比较，C组MAP、心率水平波动较小。见表2。

2.2 三组术后静息和运动状态VAS评分比较 三组

术后静息状态、运动状态VAS评分时间效应、组间效应及组间×时间交互效应，均有统计学意义（P<0.01）。两两比较，C组VAS评分较低（P<0.05）。见表3。

2.3　三组术后RSS评分比较　三组术后RSS评分时间效应、组间效应及组间×时间交互效应，均有统计学意义（P <0.01）。两两比较，C组RSS评分较高（P<0.05）。见表4。

2.4　三组术后镇痛药使用情况比较　三组术后首次追加镇痛药时间的比较，差异有统计学意义（F = 178.640，P <0.01）；与A组术后第1次追加镇痛药时间相比，B组和C组的时间延长（P<0.05），与B组相比，C组的时间延长（P<0.05）。三组追加镇痛药次数比较，差异有统计学意义（P<0.01）。A组术后追加镇痛药次数高于B组和C组（Z=3.992，P<0.01；Z=5.468，P<0.01），C组和B组比较差异无统计学意义（Z=1.834，P=0.067）。见表5。

2.5　三组药物不良反应情况　A组、B组和C组患者药物不良反应总发生率的比较，差异无统计学意义（χ^2=1.688，P=0.430）。见表6。

2.6　三组术后CPSP发生情况　A组失访1例，予以剔除，剩余31例，B、C组无失访患者。术后6个月A、B、C三组的CPSP发生率分别为19.35%（6/31）、3.13%（1/32）、0，三组比较差异具有统计学意义（χ^2=9.915，P=0.007）；与A组相比，C组的CPSP发生率较低（P<0.05），B组与C组的CPSP发生率差异无统计学意义（P>0.05）。

表1　三组一般资料情况比较　（n=32，$\bar{x}\pm s$）

Tab.1　Comparison of general data among three groups　（n=32，$\bar{x}\pm s$）

组别	年龄（岁）	性别（男/女，例）	BMI（kg/m²）	ASA分级（例）		骶管阻滞时间（min）	手术时间（min）
				Ⅰ级	Ⅱ级		
A组	44.27±12.35	17/15	22.71±2.24	16	16	6.69±1.73	32.86±15.21
B组	45.36±12.94	13/19	23.17±2.03	18	14	6.81±1.88	32.79±15.34
C组	44.61±11.89	15/17	23.36±2.18	19	13	6.77±1.76	33.41±16.07
F/χ^2值	0.043	1.004	0.509	0.590		0.025	0.010
P值	0.988	0.605	0.677	0.745		0.995	0.999

表2　三组术中不同时间点MAP、心率比较　（n=32，$\bar{x}\pm s$）

Tab.2　Comparison of MAP and heart rate at different time points during surgery among three groups　（n=32，$\bar{x}\pm s$）

组别	MAP（mmHg）				心率（次/min）			
	T0	T1	T2	T3	T0	T1	T2	T3
A组	78.35±7.63	86.26±7.48[a]	76.16±7.02[b]	78.40±6.82[b]	65.82±6.74	70.58±7.02[a]	76.47±6.81[ab]	70.38±6.25[ac]
B组	79.76±7.71	83.51±6.89[a]	77.42±6.83[bd]	78.46±6.51[b]	65.79±6.81	68.39±6.97	71.33±6.50[ab]	69.19±7.06
C组	78.41±7.60	82.68±6.92[a]	76.50±7.13[bd]	77.53±6.95[b]	66.05±6.78	68.13±7.12	70.69±6.91[ab]	67.37±7.14
$F_{时间/组间/交互}$值	15.449/23.610/19.824				18.353/26.571/34.643			
$P_{时间/组间/交互}$值	<0.001/<0.001/<0.001				<0.001/<0.001/<0.001			

注：与本组T0比较，[a]P<0.05；与本组T1比较，[b]P<0.05；与本组T2比较，[c]P<0.05；与同时点A组比较，[d]P<0.05。

表3　三组术后不同时间静息及运动状态下VAS评分比较　（n=32，分，$\bar{x}\pm s$）

Tab.3　Comparison of VAS scores among three groups of postoperative resting and exercise states at different times　（n=32，point，$\bar{x}\pm s$）

组别	静息状态				运动状态			
	T4	T5	T6	T7	T4	T5	T6	T7
A组	2.84±1.94	2.53±1.89	2.33±1.80	1.75±1.72[a]	3.26±2.01	3.45±1.84	3.28±1.81	2.89±1.65
B组	2.31±1.67	1.83±1.36	1.38±1.27[ad]	1.26±1.06[a]	2.63±1.66	2.92±1.57	2.67±1.54	2.15±1.33[b]
C组	1.85±1.53[d]	1.80±1.50	1.36±1.25[d]	0.95±0.71[abd]	2.61±1.64	2.89±1.59	2.43±1.51[d]	1.74±1.21[abcd]
$F_{时间/组间/交互}$值	23.725/30.261/35.814				17.594/28.823/34.201			
$P_{时间/组间/交互}$值	<0.001/<0.001/<0.001				<0.001/<0.001/<0.001			

注：与本组T4比较，[a]P<0.05；与本组T5比较，[b]P<0.05；与本组T6比较，[c]P<0.05；与同时点A组比较，[d]P<0.05。

表4　三组术后RSS评分比较（n=32，分，$\bar{x}\pm s$）

Tab.4　Comparison of RSS score among three groups after surgery（n=32，point，$\bar{x}\pm s$）

组别	T4	T5	T6	T7
A组	1.53±0.42	1.82±0.36[a]	2.03±0.40[ab]	2.33±0.36[abc]
B组	2.24±0.36[d]	2.48±0.45[ad]	2.36±0.42[d]	2.39±0.35
C组	2.46±0.38[de]	2.69±0.41[ade]	2.58±0.43[de]	2.38±0.37
$F_{时间/组间/交互}$值	28.716/39.641/37.594			
$P_{时间/组间/交互}$值	<0.001/<0.001/<0.001			

注：与本组T4比较，[a]P<0.05；与本组T5比较，[b]P<0.05；与本组T6比较，[c]P<0.05；与同时点A组比较，[d]P<0.05；与同时点B组比较，[e]P<0.05。

表5　三组术后镇痛药使用情况　（n=32）

Tab.5　Use of postoperative analgesics among three groups（n=32）

组别	术后首次追加镇痛药时间（min，$\bar{x}\pm s$）	追加镇痛药次数（例）		
		0次	1次	2次
A组	348.21±74.30	6	21	5
B组	608.62±69.19[a]	22	9	1
C组	820.48±90.04[ab]	28	4	0
F/H值	178.640		33.912	
P值	<0.001		<0.001	

注：与A组比较，[a]P<0.05；与B组比较，[b]P<0.05。

表6　三组药物不良反应比较　［n=32，例（%）］

Tab.6　Comparison of adverse drug reactions among three groups［n=32，case（%）］

组别	恶心呕吐	心动过缓	皮肤瘙痒	低血压	过度镇静	总发生率（%）
A组	7（21.88）	1（3.13）	1（3.13）	1（3.13）	0	31.25
B组	3（9.38）	2（6.25）	0	0	1（3.13）	18.75
C组	5（15.63）	2（6.25）	1（3.13）	0	2（6.25）	31.25
χ^2值						1.688
P值						0.430

3　讨　论

术后疼痛是肛肠手术的一种常见并发症，其发生主要与手术造成的创伤、伤口炎症反应及肛门括约肌的痉挛状态有关[15-16]。针对术后急慢性疼痛管理，临床上麻醉药物的选取至关重要。罗哌卡因作为一种新型长效酰胺类局部麻醉药物，因其对循环及呼吸系统的影响较小，药物毒性反应较低，成为骶管阻滞麻醉的首选局部麻醉药[17-18]。由于骶管阻滞通常采用单次给药，其阻滞时间相对较短，通常需复合其他药物使用以延长药效。右美托咪定属于咪唑类化合物，具有镇静、镇痛、维持血流动力学平稳及减轻应激反应等多重药理作用[19-20]。相关研究表明，右美托咪定与罗哌卡因在镇痛方面表现出协同作用，能够减少罗哌卡因的使用量[21-22]。但右美托咪定剂量的选择是否会影响术后疼痛，有待进一步探究，本研究针对不同剂量右美托咪定联合罗哌卡因骶管阻滞麻醉对肛肠术后急慢性疼痛的影响进行分析。

本研究显示，与A组比较，B组和C组手术前后血流动力学水平波动较小；且与A组比较，B组和C组T4、T5、T6时的RSS评分升高。说明右美托咪定可维持骶管阻滞麻醉下肛肠手术后的血流动力学的稳定，并具有良好的镇静效果。究其原因，右美托咪定初期进入体内时，血药浓度处于较高水平，通过作用于血管平滑肌的α2肾上腺素受体，引起血管收缩，从而使血压升高；随着药物作用时间的延长，延髓中枢的α2肾上腺素受体被激活，减少中枢神经系统内去甲肾上腺素的释放，进而降低交感神经活性，导致血压下降和心率减缓，这一发现与郑文壮等[23]的研究结果相吻合。此外，右美托咪定还能激活脑干蓝斑核的α2受体，并促进中枢神经中γ-氨基丁酸受体的表达，同时促进去甲肾上腺激素神经的超极化，有效实现其镇静作用[24]。对比发现，C组的镇静评分显著高于B组，这表明适当增加右美托咪定的剂量能够提升镇静效果。

本研究对静息及运动状态下术后VAS评分变化情况进行分析，结果提示右美托咪定联合罗哌卡因能有效缓解患者术后急性疼痛，同时发现右美托咪定联合罗哌卡因能延长镇痛持续时间，并能减少术后镇痛药的使用，且高剂量的右美托咪定镇痛效果更佳。分析原因为，右美托咪定通过与脊髓背角神经元的突触前α2受体结合，抑制去甲肾上腺素的释放，同时激活突触后α2受体介导的G蛋白打开钾离子内流通道，两者共同促使细胞超极化，进而阻断疼痛信号的传导[25-26]。高剂量的右美托咪定能更充分地占据这些受体，从而加强对疼痛信号的抑制作用；另一方面，右美托咪定还可通过外周机制发挥镇痛作用，其能抑制外周神经元的过度兴奋，并减少炎症介质的释放，尤其是高剂量右美托咪定在外周神经系统中可能具有更强的抗炎和镇痛效果，进一步延长术后镇痛的持续时间[27]。此外，本研究中A组在术后6个月时CPSP发生率低于C组，表明右美托咪定有助于改善肛肠手术后慢性疼痛的发生，可能是由于预先镇痛能够减轻外周神经感受器所受疼痛刺激的程度，进而降低外周及中枢神经系统的敏感性。但本研究受限于较小的样本量及相对短暂的随访时间，未来将扩大样本容量并延长随访期限以深入探究右美托咪定对肛肠手术后慢性疼痛管理作用。本研究结果显示，C组过度镇静的发生率略高于其他两组，这与右美托咪定在高浓度状态下，能够增强对α2肾上腺素受体的激动作用，进而过度抑制去甲肾上

腺素的释放过程有关;该作用机制致使交感神经兴奋性显著降低,促使觉醒与睡眠的动态平衡向深度镇静方向偏移。这提示在肛肠手术的麻醉管理中,临床医师需充分考量镇痛需求与镇静风险之间的关系。通过制定个体化的用药剂量方案,并实施持续性的动态监测,有助于实现镇静深度与安全性之间的优化平衡。此外,三组患者在不良反应总发生率方面比较差异无统计学意义,这一结果提示,右美托咪定联合罗哌卡因骶管阻滞麻醉对肛肠术后疼痛患者治疗方案中,安全性良好。

综上所述,右美托咪定联合罗哌卡因骶管阻滞麻醉对肛肠术后患者效果显著,不仅能够维持患者血流动力学的稳定,还展现出良好的镇静效果,对术后急性疼痛效果显著,并减少术后镇痛药的使用频率,同时具有较高的安全性,其中较高剂量的右美托咪定在此联合应用中显示出更为优越的效果。

利益冲突　无

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