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# 盐酸右美托咪定联合依托咪酯麻醉对宫腔镜手术患者血流动力学、炎症反应及氧化应激水平的影响*

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**摘要 目的:**研究盐酸右美托咪定联合依托咪酯麻醉对宫腔镜手术患者血流动力学、炎症反应及氧化应激水平的影响。**方法:**选取我院于2020年4月~2020年8月期间收治的96例择期行宫腔镜手术患者，根据住院号奇偶顺序将患者分为对照组和研究组，各48例。对照组麻醉中使用瑞芬太尼、顺阿曲库铵联合依托咪酯,研究组麻醉中使用瑞芬太尼、顺阿曲库铵、盐酸右美托咪定联合依托咪酯。对比两组麻醉诱导时间、苏醒时间、离室时间、手术时间。观察两组患者血流动力学、炎症反应及氧化应激变化。观察两组镇静、镇痛情况。记录围术期不良反应的发生情况。**结果:**研究组麻醉诱导时间短于对照组($P$<0.05)。研究组麻醉诱导后(T2)~手术结束时(T5)时间点HR、MAP均高于对照组($P$<0.05)。与对照组相比,研究组术后1 d血清白介素-6(IL-6)、肿瘤坏死因子-α(TNF-α)、C反应蛋白(CRP)水平更低($P$<0.05)。与对照组相比,研究组术后1 d过氧化氢($H_2O_2$)、丙二醛(MDA)水平更低,总抗氧化态(TAS)水平更高($P$<0.05)。研究组术后6 h、术后12 h视觉模拟评分法(VAS)评分低于对照组($P$<0.05)。研究组术后6 h、术后12 h的Ramsay镇静评分高于对照组($P$<0.05)。两组不良反应总发生率对比差异无统计学意义($P$>0.05)。**结论:**盐酸右美托咪定联合依托咪酯麻醉用于宫腔镜手术中,镇静、镇痛效果确切,在维持血流动力学稳定、减轻炎症反应及氧化应激方面效果显著。

**关键词:**盐酸右美托咪定;依托咪酯;宫腔镜;血流动力学;炎症反应;氧化应激

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# The Effect of Dextrometramidine Hydrochloride Combined with Etomidate Anesthesia on Hemodynamics, Inflammatory Response and Oxidative Stress Level in Patients Undergoing Hysteroscopy*

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**ABSTRACT Objective:** To study the effects of dextrometramidine hydrochloride combined with etomidate on hemodynamics, inflammatory response and oxidative stress in patients undergoing hysteroscopy. **Methods:** 96 patients who were treated in our hospital from April 2020 to August 2020 were selected for hysteroscopy. According to the order of hospital number parity, the patients were divided into control group and study group, 48 patients each. Remifentanil, CIS atracurium and etomidate were used in the control group, and remifentanil, CIS atracurium and dextrometramidine hydrochloride were used in the study group. The induction time, recovery time, time of departure and operation time were compared. The changes of hemodynamics, inflammatory response and oxidative stress were observed in the two groups. The sedative and analgesic conditions of the two groups were observed. The adverse reactions were recorded during the perioperative period. **Results:** The induction time of anesthesia in the study group was shorter than that of the control group ($P$<0.05). HR and MAP in the study group were higher than those in the control group from after anesthesia induction (T2) ~ at the end of operation (T5) ($P$<0.05). Compared with the control group, the serum levels of interleukin-6 (IL-6), tumor necrosis factor-α(TNF-α), C reactive protein (CRP) in the study group were significantly lower at 1d after operation($P$<0.05). Compared with the control group, the serum levels of hydrogen peroxide ($H_2O_2$) and malondialdehyde (MDA) in the study group were significantly lower ,antioxidant state (TAS) were significantly higher at 1 d after operation ($P$<0.05). The visual analogue scale (VAS) score of the study group was lower than that of the control group at 6 h and 12 h after operation ($P$<0.05). Ramsay Sedation scores of the study group at 6 h and 12 h after operation were higher than those of the control group ($P$<0.05). There was no significant difference in the total incidence of adverse reactions between the two groups ($P$>0.05). **Conclusion:** The sedative and analgesic effects of dextrometropidine hydrochloride combined with etomidate anesthesia in hysteroscopy are accurate, and have significant effects on maintaining

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hemodynamic stability, reducing inflammation and oxidative stress.

**Key words:** Dextrometramidine hydrochloride; Etomidate; Hysteroscopy; Hemodynamics; Inflammatory response; Oxidative stress
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## 前言

随着微创技术的发展,宫腔镜手术因其术后创伤小、恢复快、并发症少,同时对患者呼吸与循环系统的影响轻微等特点广泛应用于妇科疾病的治疗中[1]。然而术中使用钳刮扩张宫颈口、插入内窥器等操作仍可使患者产生不同程度的疼痛[2]。而疼痛可使患者躁动,甚至扭动躯体,增加手术难度[3]。因此,优质的麻醉是保障手术顺利完成的基础。依托咪酯是临床广泛使用的一种镇静催眠药,具有呼吸抑制轻微、无注射痛等优点,但依托咪酯麻醉可引起肌肉震颤等不良反应[4]。盐酸右美托咪定具有良好的镇痛、镇静效果,且无呼吸抑制,同时可减少其他镇静药物的用量,近年来在临床麻醉中受到的关注度越来越高[5,6]。本研究对宫腔镜手术患者麻醉中使用盐酸右美托咪定联合依托咪酯方案,效果良好,整理报道如下。

## 1 资料与方法

### 1.1 一般资料

选取我院于 2020 年 4 月 ~2020 年 8 月期间收治的 96 例择期行宫腔镜手术患者,年龄 25~58(39.27±5.19)岁;体质量 40~80(56.50±3.94)kg;美国麻醉医师协会(ASA)[7]分级:Ⅰ级 51 例,Ⅱ级 45 例;其中子宫黏膜下肌瘤 38 例,子宫内膜息肉 36 例,功能性子宫出血 22 例。研究方案通过我院伦理学委员会批准。纳入标准:(1)符合宫腔镜手术指征者;(2)ASA 分级Ⅰ~Ⅱ级者;(3)签署知情同意书。排除标准:(1)存在药物成瘾史者;(2)心、肾、肺等器官检查存在异常者;(3)对本研究药物过敏患者;(4)具有精神障碍者;(5)血常规、血生化指标明显异常者。根据住院号奇偶顺序将患者分为对照组和研究组,各 48 例。对照组年龄 25~56(39.62±4.18)岁;体质量 40~79(56.29±3.87)kg;ASA 分级:Ⅰ级 25 例,Ⅱ级 23 例;其中子宫黏膜下肌瘤 20 例,子宫内膜息肉 17 例,功能性子宫出血 11 例。研究组年龄 26~58(38.91±5.26)岁;体质量 42~80(56.70±4.06)kg;ASA 分级:Ⅰ级 26 例,Ⅱ级 22 例;其中子宫黏膜下肌瘤 18 例,子宫内膜息肉 19 例,功能性子宫出血 11 例。两组一般资料组间对比无统计学差异($P$>0.05),具有可比性。

### 1.2 方法

(1)麻醉前准备:术前 1d 访视患者,充分了解患者的健康状况、精神状态,并对患者进行血尿粪三大常规检查,获取凝血功能、血生化检查、心电图及影像学等检查结果,取得患者及其家属的知情同意与配合。术前常规禁饮 4h,禁食 8h,术前 30 min 肌注 0.5 mg 硫酸阿托品注射液(规格:1 mL: 5 mg,国药准字 H32022467,江苏悦兴药业有限公司生产)。入室前开通前臂的静脉通道,入室后核对并确认患者信息,随后,连接 BeneVision N22 型病人监护仪(深圳迈瑞生物医疗电子股份有限公司生产)监测心电图、平均动脉压(MAP)、心率(HR)。(2)麻醉方法:两组均采用喉罩置入全身麻醉,入手术室后给予 2 L/min 的面罩给氧,对照组给予泵注注射用盐酸瑞芬太尼(瑞捷)[规格:1 mg(以 $C_{20}H_{28}N_2O_5$ 计),(国药准字 H20030200,宜昌人福药业有限责任公司生产]10 μg/kg,输注时间 10 min;依托咪酯注射液(规格:10 mL: 20 mg,国药准字 H32022992,江苏恩华药业股份有限公司生产)0.2 mg/kg,注射用苯磺顺阿曲库铵[规格:5 mg,国药准字 H20060927,上药东英(江苏)药业有限公司生产]0.15 mg/kg 静脉注射后,微量泵静脉泵入注射用盐酸瑞芬太尼 0.07~0.10 μg/kg·min 和依托咪酯注射液 0.6~0.8 mg/kg·h 维持麻醉。研究组给予静脉泵注盐酸右美托咪定注射液[规格:2 mL: 200 μg(按右美托咪定计),国药准字 H20090248,江苏恒瑞医药股份有限公司生产)]1 μg/kg,输注时间 10 min,泵注注射用盐酸瑞芬太尼 10 μg/kg,输注时间 10 min,依托咪酯注射液 0.2 mg/kg,注射用苯磺顺阿曲库铵0.15 mg/kg 静脉注射后,微量泵静脉泵入注射用盐酸瑞芬太尼 0.07~0.10 μg/kg·min,盐酸右美托咪定注射液 0.3~0.4 μg/kg·h 和依托咪酯注射液 0.6~0.8 mg/kg·h 维持麻醉。每组均根据需要间断追加肌松药注射用苯磺顺阿曲库铵 0.03 mg/kg,并于手术结束前 5 min 停药。手术中 HR<50 次/min 时静注阿托品 0.1~0.3 mg,MAP<60 mmHg 静注麻黄碱 5~10 mg。术后送至麻醉后恢复室进行复苏。

### 1.3 评价指标

(1)观察两组患者麻醉诱导时间、苏醒时间(停药至呼唤睁眼)、离室时间(从睁眼至离室的时间)、手术时间。(2)记录患者手术前(T1)、麻醉诱导后(T2)、扩宫时(T3)、清除肿物时(T4)、手术结束时(T5)、手术结束 10 min 时(T6)的 MAP、HR 情况。(3)于 T1、术后 1 d 采集两组血液标本 4 mL,采血后 40 min 内室温送检,选用科大创新股份有限公司中佳分公司生产的高速台式离心机(KDC-16H 型),经 3400 r/min 离心 12 min,离心半径 14 cm,分离上清液,置于医用超低温冷冻箱(日本 SANYO 公司生产,MDF-1156 型)中待检。采用酶联免疫吸附试验检测白介素 -6(IL-6)、肿瘤坏死因子 -α(TNF-α)、C 反应蛋白(CRP)以及过氧化氢($H_2O_2$)、丙二醛(MDA)和总抗氧化态(TAS),试剂盒购自上海酶联生物科技有限公司。(4)记录两组患者术后 1h、术后 6h、术后 12h 的视觉模拟评分法(VAS)[8]评分和 Ramsay 镇静评分[9],VAS 评分 0~10 分,患者根据自己的疼痛程度进行选择,0 分为无痛,10 分为最剧烈疼痛。Ramsay 镇静评分 1~6 分,1 分为焦虑;2 分为配合,安静;3 分患者对指令有反应;4 分为浅睡眠状态;5 分为嗜睡;6 分为深睡。(5)记录两组不良反应如恶心、术后呕吐、嗜睡、肌肉震颤、心动过缓发生情况。

### 1.4 统计学方法

所得数据采用 SPSS26.0 统计软件进行分析。临床指标、血流动力学指标等计量资料以均数±标准差($\bar{x}\pm s$)表示,组内两个时点(配对 t 检验)+ 多时间点重复观测资料(F 检验),两组比较(独立 t 检验),两两比较采用最小显著差法(LSD-t)和差值 t

检验法。性别、不良反应等计数资料以%表示，比较采用 $\chi^2$ 检验。检验水准 $\alpha$=0.05(双侧检验)。

## 2 结果

### 2.1 两组临床指标对比

两组苏醒时间、离室时间、手术时间组间对比差异未见统计学意义($P$>0.05)，研究组麻醉诱导时间短于对照组($P$<0.05)，具体见表 1。

表 1 两组临床指标对比($\bar{x}\pm s$，min)

Table 1 Comparison of clinical indexes between the two groups($\bar{x}\pm s$，min)

| Groups | Anesthesia induction time | Recovery time | Time out of room | Operation time |
|---|---|---|---|---|
| Control group(n=48) | 3.26±0.67 | 7.52±0.34 | 10.85±0.63 | 33.71±2.79 |
| Study group(n=48) | 2.17±0.48 | 7.44±0.52 | 10.66±0.48 | 32.83±3.92 |
| t | 9.163 | 0.892 | 1.662 | 1.267 |
| $P$ | 0.000 | 0.375 | 0.100 | 0.208 |

### 2.2 两组血流动力学指标对比

研究组各时间点 HR、MAP 比较差异无统计学意义($P$>0.05)。对照组 T2、T3、T4 时间点 HR、MAP 均较 T1 时间点降低($P$<0.05)。研究组 T2~T5 时间点 HR、MAP 均高于对照组($P$<0.05)。详见表 2。

表 2 两组血流动力学指标对比($\bar{x}\pm s$)

Table 2 Comparison of hemodynamic indexes between the two groups($\bar{x}\pm s$)

| Groups | Time | HR(n/min) | MAP(mmHg) |
|---|---|---|---|
| Control group(n=48) | T1 | 88.14±8.62 | 85.82±5.94 |
| | T2 | 78.86±7.47$^{t}$ | 73.84±6.87$^{t}$ |
| | T3 | 78.57±6.43$^{t}$ | 75.69±6.07$^{t}$ |
| | T4 | 81.09±7.53$^{t}$ | 78.27±6.19$^{t}$ |
| | T5 | 87.21±6.47 | 84.91±7.40 |
| | T6 | 87.31±7.05 | 86.57±7.30 |
| Study group(n=48) | T1 | 87.73±7.28 | 86.39±7.58 |
| | T2 | 89.45±8.23$^{a}$ | 87.03±6.56$^{a}$ |
| | T3 | 88.33±9.37$^{a}$ | 86.41±5.24$^{a}$ |
| | T4 | 89.00±8.25$^{a}$ | 88.57±6.35$^{a}$ |
| | T5 | 86.88±7.90 | 87.22±6.64 |
| | T6 | 88.39±6.59 | 86.64±7.91 |
| Overall analysis | HF | 1.0136 | 0.8983 |
| Comparison between groups | F,$P$ | 43.112,0.000 | 173.684,0.000 |
| Comparison intra group | F,$P$ | 6.647,0.000 | 14.969,0.000 |
| Interaction | F,$P$ | 11.796,0.000 | 17.180,0.000 |

Note: significant marker t is compared with T1 time point in group, $P<\alpha'$,$\alpha'$ Test level after Bonferroni correction = 0.05/5 = 0.01, compared with the control group, $^{A}P$<0.05.

### 2.3 两组炎症反应指标水平对比

术后 1 d，两组血清 IL-6、TNF-α、CRP 水平均较 T1 时间点升高（$P$<0.05），与对照组相比，研究组术后 1 d 血清 IL-6、TNF-α、CRP 水平更低($P$<0.05)，详见表 3。

### 2.4 两组氧化应激反应指标水平对比

术后 1d，两组 MDA、$H_2O_2$ 水平均较 T1 时间点升高，TAS 水平均较 T1 时间点降低($P$<0.05)，与对照组相比，研究组术后 1 d 的 $H_2O_2$、MDA 水平更低，TAS 水平更高($P$<0.05)，详见表 4。

### 2.5 两组镇痛、镇静评分对比

术后 6 h、术后 12 h，两组 VAS 评分呈降低趋势，且研究组术后 6 h、术后 12 h 的 VAS 评分低于对照组($P$<0.05)。术后 6 h、术后 12 h，对照组 Ramsay 镇静评分呈降低趋势($P$<0.05)。术后 6 h、术后 12 h，研究组 Ramsay 镇静评分与术后 1 h 对比差异无统计学意义($P$>0.05)。研究组术后 6 h、术后 12 h 的 Ramsay 镇静评分高于对照组($P$<0.05)，详见表 5。

### 2.6 两组不良反应发生情况对比

对照组的不良反应总发生率为 14.58%(7/48)，研究组的

表 3 两组炎症反应指标水平对比($\bar{x}\pm s$)

Table 3 Comparison of inflammatory reaction indexes between the two groups($\bar{x}\pm s$)

| Groups | Time | IL-6(ng/L) | TNF-α(ng/mL) | CRP(mg/L) |
|---|---|---|---|---|
| Control group | T1 | 218.73±25.86 | 9.31±1.63 | 7.37±1.24 |
| n=48 | 1d after operation | 355.32±32.54 | 26.75±3.51 | 17.96±1.18 |
| | Difference | 136.59±23.33 | 17.44±2.12 | 10.59±2.92 |
| | t,*P* | 40.563,0.000 | 56.994,0.000 | 25.127,0.000 |
| Study group | T1 | 217.51±34.62 | 9.38±1.29 | 7.31±1.08 |
| n=48 | 1d after operation | 292.89±36.52 | 15.58±4.82 | 12.39±1.29 |
| | Difference | 75.38±70.27 | 6.20±3.76 | 5.08±0.69 |
| | t,*P* | 7.432,0.000 | 11.424,0.000 | 51.008,0.000 |
| Comparison between the two groups(t,*P*) | T1 | 0.196,0.845 | 0.233,0.816 | 0.253,0.801 |
| | 1d after operation | 8.843,0.000 | 12.979,0.000 | 22.073,0.000 |

表 4 两组氧化应激反应指标水平对比($\bar{x}\pm s$)

Table 4 Comparison of oxidative stress indexes between the two groups($\bar{x}\pm s$)

| Groups | Time | $H_2O_2$(mmol/L) | MDA(nmol/L) | TAS(ng/L) |
|---|---|---|---|---|
| Control group | T1 | 36.48±4.32 | 5.18±0.65 | 193.75±18.55 |
| n=48 | 1d after operation | 62.35±5.74 | 8.91±0.86 | 125.92±18.26 |
| | Difference | 25.87±9.84 | 3.73±1.08 | -67.83±11.68 |
| | t,*P* | 18.215,0.000 | 23.928,0.000 | 40.235,0.000 |
| Study group | T1 | 36.30±3.95 | 5.23±0.42 | 192.34±21.04 |
| n=48 | 1d after operation | 51.09±4.52 | 6.13±0.47 | 164.31±23.79 |
| | Difference | 14.79±2.45 | 0.90±0.52 | -28.03±44.28 |
| | t,*P* | 41.824,0.000 | 11.991,0.000 | 4.386,0.000 |
| Comparison between the two groups(t,*P*) | T1 | 0.213,0.832 | 0.448,0.655 | 0.348,0.729 |
| | 1d after operation | 10.678,0.000 | 19.652,0.000 | 8.869,0.000 |

表 5 两组镇痛、镇静评分对比($\bar{x}\pm s$,分)

Table 5 Comparison of analgesic and sedative scores between the two groups($\bar{x}\pm s$,score)

| Groups | Time | VAS | Ramsay |
|---|---|---|---|
| Control group(n=48) | 1h after operation | 1.68±0.25 | 2.76±0.28 |
| | 6h after operation | 4.00±0.35[t] | 2.11±0.28[t] |
| | 12h after operation | 2.73±0.26[t] | 1.57±0.15[t] |
| Study group(n=48) | 1h after operation | 1.70±0.28 | 2.76±0.25 |
| | 6h after operation | 3.26±0.38[at] | 2.65±0.25[at] |
| | 12h after operation | 2.08±0.18[at] | 2.60±0.19[at] |
| Overall analysis | HF | 0.9377 | 0.7740 |
| Comparison between groups | F,*P* | 184.907,0.000 | 310.292,0.000 |
| Comparison intra group | F,*P* | 1,045.141,0.000 | 208.736,0.000 |
| Interaction | F,*P* | 46.421,0.000 | 121.220,0.000 |

为 18.75%(9/48),组间对比差异无统计学意义(*P*>0.05)。详见表 6。

## 3 讨论

手术会对机体造成强烈的刺激从而产生局部炎症反应和

表 6 两组不良反应发生率对比[例(%)]

Table 6 Comparison of the incidence of adverse reactions between the two groups[n(%)]

| Groups | Postoperative vomiting | Nausea | Muscle tremor | Drowsiness | Bradycardia | Total occurrence rate |
|---|---|---|---|---|---|---|
| Control group (n=48) | 2 | 1 | 2 | 1 | 1 | 7(14.58) |
| Study group(n=48) | 2 | 2 | 3 | 1 | 1 | 9(18.75) |
| $\chi^2$ | | | | | | 0.300 |
| *P* | | | | | | 0.584 |

氧化应激等应激反应，而强烈的应激反应可导致交感 - 肾上腺髓质系统受到刺激，释放大量的儿茶酚胺，造成全身血液循环加快，引起血压、HR 等发生剧烈波动[10,11]；同时强烈的应激反应还可导致躯体敏感化，致使患者疼痛敏感度提高，不利于手术的顺利进行[12]。依托咪酯为咪唑类衍生物，具有作用迅速而短暂、苏醒快、中枢神经抑制作用强等优点[13]。其麻醉作用的分子机制目前尚不十分明确，不少学者认为其与 γ- 氨基丁酸受体的调节作用有关[14,15]。但依托咪酯的镇痛效果相对轻微，同时单独使用时易导致肌肉震颤、恶心呕吐等不良反应[16]。瑞芬太尼为芬太尼类 μ 型阿片受体激动剂，此类麻醉药物起效迅速、可控性强、镇痛作用明显[17]。但瑞芬太尼也具备阿片类药物常见的不良反应如 HR 减慢和呼吸抑制等。盐酸右美托咪定主要通过作用于外周和中枢神经的肾上腺素能受体发挥镇静、镇痛作用，近年来在麻醉中得到了广泛应用[18]。

本次研究结果显示，相比于瑞芬太尼、顺阿曲库铵联合依托咪酯麻醉，宫腔镜手术中应用瑞芬太尼、顺阿曲库铵、盐酸右美托咪定联合依托咪酯麻醉，镇静、镇痛效果良好，在缩短麻醉诱导时间、稳定血流动力学方面同样具有较好的改善意义。盐酸右美托咪定主要通过与 α2 肾上腺素能受体结合发挥药理作用，而 α2 中又包括 3 个亚型 α2-A、α2-B、α2-C，每个亚型分布及激动后效应均不同[19]。α2-A 受体主要集中于脑干的蓝斑核，而脑干的蓝斑核可有效调节人体的睡眠、觉醒以及各项疼痛刺激[20]。α2-B 受体主要集中于血管平滑肌，可介导盐酸右美托咪定的 MAP 调节作用[21]。α2-C 主要集中于脊髓后角，可介导盐酸右美托咪定的镇静作用[22]。同时，盐酸右美托咪定不通过 γ- 氨基丁酸起效，不会引起自主活动的抑制，更利于依托咪酯发挥麻醉作用，缩短麻醉诱导时间[23]。

手术创伤可使血液中炎症因子过度释放，氧自由基大量生成，从而引起机体的过度炎性反应和氧化应激，使术后并发症增加[24]。细胞因子是一种有调节功能的活性多肽类物质，其中 $H_2O_2$ 是体内的一种活性氧存在形式，可促进自由基生成[25]；TAS 可反映机体总抗氧化能力[26]；MDA 是脂质过氧化的产物，可反映机体组织损伤程度[27]。TNF-α 是机体损伤期间宿主反应较早的炎性介质，可引起机体全身炎性反应[28]；IL-6 是多种生物学效应的促炎因子[29]，CRP 则是炎症反应的重要标志[30]，其水平的高低与炎症程度呈正相关。本次研究结果中，瑞芬太尼、顺阿曲库铵、盐酸右美托咪定联合依托咪酯麻醉，可减轻人体的炎性反应和氧化应激。以往的研究证实[31]，盐酸右美托咪定可降低机体自由基水平，减轻氧化应激损伤。而有关盐酸右美托咪定在手术期间抗炎作用的机制尚不十分明确，可能与突触前 α2 肾上腺素能受体有关[19]。此外，本研究还观察了两组不良反应总发生率，结果表明，宫腔镜手术中应用瑞芬太尼、顺阿曲库铵、盐酸右美托咪定联合依托咪酯麻醉，不会增加不良反应发生率，安全可靠。

综上所述，宫腔镜手术中应用盐酸右美托咪定联合依托咪酯麻醉，镇静、镇痛效果确切，可维持患者血流动力学稳定，减轻机体应激反应且安全性较好。

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