地佐辛超前镇痛对隐匿性阴茎矫治术患儿苏醒期谵妄的临床观察

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摘 要：【目的】观察地佐辛超前镇痛对隐匿性阴茎矫治术患儿苏醒期谵妄(ED)的影响。【方法】筛选2020年7月至2020年10月62例6～10岁拟行隐匿性阴茎矫治术的男孩，按随机数字表法分为生理盐水对照组(C组，n=32例)和地佐辛组(D组，n=30例)，所有患者均采用静吸复合全麻(喉罩)。2组分别在麻醉诱导前5 min给予等容量的0.9%生理盐水10 mL或地佐辛0.1 mg/kg (0.9%生理盐水稀释至10 mL)。比较2组入PACU即刻(T_1)、10 min(T_2)、出PACU即刻(T_3)、术后1 h(T_4)、术后6 h(T_5)PAED评分及FLACC疼痛评分；比较2组术后ED、导尿管相关膀胱不适(CRBD)发生率。问卷患儿父母术后48 h内新发适应不良行为发生情况并比较；比较2组麻醉诱导前30 min(T_0)、T_1、T_4、T_5外周静脉血皮质醇(Cor)、肾上腺素(E)、血糖(Glu)水平。【结果】D组在T_2～T_5点PAED评分明显低于C组(P<0.001)；FLACC评分低于C组(P<0.001)；D组ED的发生率明显低于C组(16.67% *vs.* 40.63%，P=0.039)，术后48 h内新发适应不良行为的总发生率低于C组(13.33% *vs.* 37.50%，P=0.042)；CRBD发生率低于C组(6.67% *vs.* 28.13%，P=0.044)。D组在T_1、T_4、T_5点E、Cor、Glu水平明显低于C组(组间P值分别为P<0.001，P=0.009，P=0.012)。【结论】地佐辛超前镇痛可明显降低小儿隐匿性阴茎术后ED的发生率；降低术后新发适应不良行为的发生率，可能与地佐辛降低术后疼痛应激及CRBD的发生率有关。

关键词：地佐辛；超前镇痛；小儿；苏醒期谵妄
中图分类号：R614 **文献标志码：**A **文章编号：**1672-3554(2021)01-0102-07

Preemptive Analgesic Effects of Dezocine on Emergence Delirium in Children Undergoing Concealed Penis Correction: a Clinical Observation

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Abstract:【Objective】To observe the preemptive analgesic effects of dezocine on emergence delirium (ED) in children undergoing concealed penis correction.【Methods】Sixty-two 6~10 years old boys scheduled for concealed penis correction under general anesthesia from July 2020 to October 2020 were randomly divided into normal saline control group (Group C, n=32) and dezocine group (Group D, n=30). Five minutes before the anesthetic induction, Group C was treated with 10 mL of 0.9% normal saline and Group D with same amount of dezocine 0.1 mg/kg (diluted to 10 mL by 0.9% saline). Pediatric Anesthesia Emergence Delirium scale (PAED) scores and Face, Legs, Activity, Cry, Consolability scale (FLACC) scores of the two groups were recorded and compared at the time points of entering postanesthesia care unit (PACU) (T_1), 10 min after entering PACU (T_2), leaving PACU (T_3), 1 h (T_4) and 6 h (T_5) after the surgery. The postoperative incidence of ED and urinary catheter-related bladder discomfort (CRBD) were compared between the two groups. Newly occurred maladaptive behaviors within 48 h after surgery were documented by parents in a questionnaire and com-

收稿日期：2020-12-04
基金项目：安徽省自然科学基金(1808085MH230)；安徽省科技创新与软科学研究专项(201806a02020045)
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pared between the two groups. We also compared the levels of cortisol, epinephrine and blood glucose at 30 min before induction (T_0), T_1, T_4 and T_5 between the two groups.【Results】PAED scores and FLACC scores at T_1 to T_5 in Group D were significantly lower than those in Group C (both P<0.001). Group D had lower incidence of ED (16.67% *vs.* 40.63%, P=0.039), CRBD (6.67% *vs.* 28.13%, P=0.044) and newly occurred maladaptive behaviors within 48 h after surgery (13.33% *vs.* 37.50%, P=0.042). The levels of cortisol, epinephrine and glucose were significantly lower in Group D at T_1, T_4, T_5 (P<0.001, P=0.009 and P=0.012, respectively) than those in Group C.【Conclusions】Preemptive analgesia by using dezocine can significantly reduce the the incidence of ED and newly occurred maladaptive behaviors in children undergoing concealed penis correction, which could be explained by the fact that dezocine can reduce the postoperative pain stress and the incidence of CRBD.

Key words: dezocine; preemptive analgesia; pediatric; emergence delirium (ED)

[J SUN Yat-sen Univ(Med Sci),2021,42(1):102-108]

苏醒期谵妄(emergence delirium, ED)是小儿全麻苏醒期常见的并发症,男性患儿发生率更高,其发生机制仍不清楚,最常见的诱因包括术前焦虑、吸入麻醉药、疼痛[1],术后留置导尿管等不良刺激亦会增加ED的发生率[1-2]。ED不仅令患儿不适,也令护理人员和家长对麻醉复苏的质量感到不满。严重者造成意外伤害,延长住院时间,部分患儿出现新的适应不良行为[1],有必要采取预防和治疗措施。超前镇痛是近年来广泛开展于临床的一种新型镇痛模式,即在伤害性刺激作用开始前采用预防性措施,减少有害刺激所致的中枢和外周敏感化,旨在降低术后痛感及镇痛药物的用量[3]。地佐辛是围麻醉期常用的辅助性镇痛药[4-6],术毕给予地佐辛能有效降低学前儿童术后ED的发生率[7];但地佐辛超前镇痛对小儿术后ED的影响尚不甚清楚。隐匿性阴茎矫治因阴茎神经分布密集,对伤害刺激反应敏感,术中及术后可产生剧烈疼痛[8-9],加之术后常规留置导尿管刺激,均是增加ED发生的高风险因素。本研究拟观察地佐辛超前镇痛对小儿隐匿性阴茎矫治术后ED的影响。

1　材料与方法

1.1　一般资料

选择2020年7月至2020年10月在安徽省儿童医院行隐匿性阴茎矫治术的小儿62例,ASA Ⅰ~Ⅱ,年龄6~10岁;体质量22~55 kg。麻醉均采用静吸复合全麻(喉罩),采用随机数字表法,分为生理盐水对照组(C组,n=32)和地佐辛组(D组,n=30)。排除标准:①患儿家属拒绝者;②智力障碍及发育迟缓者;③有地佐辛使用禁忌症者如消化性溃疡病史、血小板功能异常及凝血障碍等;④合并其他重要器官疾患者。本研究经医院医学伦理委员会批准,患儿监护人签署知情同意书。

1.2　麻醉方法

常规禁食水,无术前麻醉用药,在病房开放外周静脉通路。入室前,采用改良Ramsay镇静量表(Modified Ramsay score scale, MRS)评估焦虑水平,常规监测NIBP、HR、S_pO_2、$P_{ET}CO_2$、体温及心电图。根据分组情况给予提前配制好的9 g/L生理盐水10 mL或地佐辛溶液(扬子江药业公司,国药准字H20080329,批号:20052121,0.1 mg/kg,9 g/L生理盐水稀释至10 mL)。5 min后开始麻醉诱导:静注戊乙奎醚0.01 mg/kg、丙泊酚2~3 mg/kg、舒芬太尼0.3~0.4 μg/kg、罗库溴铵0.3~0.5 mg/kg、地塞米松0.1 mg/kg,下颌完全松弛后置入喉罩,行压力控制通气,根据年龄设置呼吸参数:吸气压力(PIP)12~15 cmH_2O,RR14~20 bpm,维持潮气量8~10 mL/kg,$P_{ET}CO_2$ 30~35 mmHg。麻醉维持:吸入1.5%~2%七氟醚(氧流量2 L/min,维持患儿呼气末七氟烷浓度于1 MAC);静脉泵注右美托咪定,负荷量1 μg/kg,10 min输完,继之维持量每小时0.5 μg/kg;瑞芬太尼每分钟0.25 μg/kg。术中根据血流动力学监测值调整输液量及输液速度。术毕外科医生行阴茎背根神经阻滞(dorsal penile nerve block, DPNB),给予体积分数1%利多卡因复合0.25%罗哌卡因混合液0.1 mL/kg,置入年龄相应的导尿管,手术结束前逐渐减浅麻醉至停药,自主呼吸恢复良好,拔喉罩转入PACU。

1.3 观察指标

在入PACU即刻(T_1)、10 min(T_2)、出PACU即刻(T_3)、术后1 h(T_4)、6 h(T_5)评测小儿苏醒期谵妄(Pediatric Anesthesia Emergence Delirium, PAED)量表[10]评分,FLACC疼痛评分。留取麻醉诱导前30 min(T_0)、T_1、T_4、T_5外周静脉血3 mL,离心取血清冻存,待统一检测血皮质醇(Cortisol, Cor)、肾上腺素(Epinephrine, E)、血糖(Glucose, Glu)水平。问卷患儿父母术后48 h新的适应不良行为发生情况。记录术后导尿管相关膀胱不适(CRBD)以及恶心、呕吐、嗜睡等不良反应发生率。PAED量表5项总分共20分,得分越高,苏醒期躁动倾向性越大,总分≥10分认为发生临床意义的ED[11];当FLACC评分≥4分,追加镇痛药物治疗,如在PACU静注舒芬太尼0.1 μg/kg,在病房则静注酮咯酸氨丁三醇0.5 mg/kg,最大不超过15 mg,记录两组术后6 h内追加镇痛药的例数;并记录两组各时间点MAP、HR。术前改良Ramsay评分(按清醒焦虑到完全没有反应共分为8个等级,记1~8分)

1.4 统计学方法

应用SPSS 20.0软件对数据进行统计分析,符合正态分布计量资料以($\bar{x} \pm s$)表示,两组间均数比较采用t检验;非正态分布计量资料以M(P_{25}~P_{75})表示,组间比较采用非参数Mann-Whitney U检验;重复测量资料采用重复测量方差分析,当Mauchly's检验数据不满足球形假设条件,采用Greenhouse-Geisser校正,多重比较采用Bonferroni法(校正后的$\alpha' = \alpha$/比较次数);计数资料用n(%)表示,组间比较采用χ^2检验或Fisher's确切概率法;以P<0.05为差异具有统计学意义。

2 结 果

2.1 一般资料比较

两组患儿年龄、体质量、手术时间、麻醉时间及术前MRS评分等一般资料进行比较,差异无统计学意义(P>0.05),具可比性。2组术后均无苏醒延迟,D组PACU停留时间明显短于C组(P<0.05;表1-2)。

表1 两组患儿一般资料

Table 1 The comparison of demographic date in two groups ($\bar{x} \pm s$)

Groups	Age/years	Weight/kg	Duration of surgery/min	Duration of anesthesia/min	PACU stay /min
C(n=32)	8.35±1.02	38.36±9.04	30.81±9.68	54.09±8.84	21.41±5.81
D(n=30)	8.45±0.96	37.97±8.61	31.06±11.81	55.46±11.40	17.44±5.19
t	0.397	0.174	0.091	0.531	−2.831
P	0.693	0.863	0.928	0.598	0.006

表2 两组患儿术前MRS比较(等级分)

Table 2 The comparison of preoperative modified Ramsay score in two groups (Grade) (n)

Groups	Cases	Grade One	Grade Two	Grade Three
C	32	5	25	2
D	30	4	21	5

MRS: modified Ramsay score, tested by Mann-Whitney U, Z=0.943, P=0.346

2.2 术中各时间点MAP、HR的比较

两组患儿MAP组间比较差异有统计学意义(F=4.53, P=0.037),两两比较的结果显示:与T_1点比较,2组在T_2点差异均有统计学意义(C组:P<0.000 1,D组:P=0.042 5);与C组相比,D组T_2点差异有统计学意义(P=0.001 2);余无统计学意义。两组患儿HR组间比较差异有统计学意义(F=4.84, P=0.032),两两比较的结果显示:与T_1点比较,2组在T_2点差异有统计学意义(C组:P<0.000 1,D组:P=0.001 8);与C组相比,D组T_2点差异有统计学意义(P=0.006 8);余无统计学意义(表3)。

2.3 不同时间点PAED、FLACC值比较

两组患儿PAED评分组间比较差异有统计学意义(F=29.18, P<0.001),两两比较的结果显示:与T_1点比较,两组PAED、FLACC值在T_2~T_5均明显增

表3　两组各时间点MAP、HR的比较

Table 3　The comparison of MAP and HR at various time points between two groups　($\bar{x} \pm s$)

Parameter	Groups	T_1	T_2	T_3	T_4	T_5
MAP/mmHg	C（n=32）	71.53±7.04	81.60±5.02[1)]	77.16±10.36	77.63±7.05	74.25±7.38
	D（n=30）	70.60±8.73	75.36±9.04[1)2)]	73.50±10.02	72.30±9.78	71.83±7.58
	$F_{Groups/Factor/Factor\ interaction}$	4.53/17.07/2.55				
	$P_{Groups/Factor/Factor\ interaction}$	0.037/<0.001/<0.04				
HR/bpm	C（n=32）	67.16±6.19	78.41±8.47 [1)]	74.78±7.01	72.19±7.65	69.34±6.24
	D（n=30）	66.90±6.14	72.70±7.51 [1)2)]	71.53±5.86	69.33±4.59	64.87±3.15
	$F_{Groups/Factor/Factor\ interaction}$	4.84/51.98/3.86				
	$P_{Groups/Factor/Factor\ interaction}$	0.032/<0.001/<0.005				

Compare with T_1, [1)]$P<0.05$, compare with group C, [2)]$P<0.05$. MAP: mean arterial pressure ; HR: heart rate

高（P<0.05），T_2时最高；与C组相比，D组T_2～T_5点差异均有统计学意义（P=0.000 2，P<0.000 1，P<0.000 1，P<0.000 1）。两组患儿FLACC评分组间比较差异有统计学意义（F=22.95，P<0.001），两两比较的结果显示：与T_1点比较，两组FLACC值在T_2～T_5均明显增高，差异均有统计学意义（P<0.05），且T2时最高；与C组相比，D组T_2～T_5点差异均有统计学意义（P=0.006，P<0.000 1，P<0.000 1，P<0.000 1，表4）。

2.4　不同时间点E、Cor、Glu值比较

两组患儿E组间比较差异有统计学意义（F=33.45，P<0.001），两两比较的结果显示：与T_0点比较，T_1、T_4、T_5点2组E均明显增高，T_4点最高（P<0.05）；与C组比较，D组在T_1、T_4、T_5点E值较低，差异均有统计学意义（P<0.000 1，P<0.000 1，P<0.000 1）。两组Cor组间比较差异有统计学意义（F=7.21，P=0.009），两两比较的结果显示：与T_0点比较，T_1、T_4、T_5点2组Cor均明显增高，T_4点最高（P<0.05）；与C组比较，D组在T_1、T_4、T_5点Cor值较低，差异均有统计学意义（P<0.000 1，P=0.048 2，P=0.000 7）。两组Glu组间比较差异有统计学意义（F=6.78，P=0.012），两两比较的结果显示：与T_0点比较，T_1、T_4、T_5点2组Glu值明显增高，T_4点最高（P<0.05）；与C组比较，D组在T_1、T_4、T_5点Glu值较低，差异均有统计学意义（P=0.040 6，P=0.013 7，P=0.003 2，表5）。

表4　两组患儿各时间点PAED、FLACC值比较

Table 4　The comparison of PAED、FLACC at various time points　($\bar{x} \pm s$)

Parameter	Groups	T_1	T_2	T_3	T_4	T_5
PAED	C（n=32）	4.16±0.37	8.88±1.96[1)]	7.53±1.41[1)]	6.91±1.17[1)]	6.00±1.42[1)]
	D（n=30）	4.20±0.48	6.77±2.11[1)2)]	5.76±1.41[1)2)]	5.37±1.47[1)2)]	4.13±0.35[2)]
Scroes	$F_{Groups/Factor/Factor\ interaction}$	29.18/136.73/12.84				
	$P_{Groups/Factor/Factor\ interaction}$	<0.001/<0.001/<0.001				
FLACC	C（n=32）	0.38±0.49	3.78±1.45[1)]	3.63±0.94[1)]	3.53±0.62[1)]	3.03±0.78[1)]
	D（n=30）	0.33±0.61	2.77±1.22[1)2)]	2.47±0.94[1)2)]	2.33±0.80[1)2)]	2.13±0.82[1)2)]
Scroes	$F_{Groups/Factor/Factor\ interaction}$	22.95/213.91/8.46				
	$P_{Groups/Factor/Factor\ interaction}$	<0.001/<0.001/<0.001				

Adjusted by greenhouse-geisser, compare with T_1, [1)]$P<0.05$, compare with group C, [2)]$P<0.05$. PAED: pediatric anesthesia emergence delirium; FLACC: face, legs, activity, cry, consolability

表5 两组患儿各时间点E、Cor、Glu值比较

Table 5 The comparison of E、Cor、Glu at various time points between two groups ($\bar{x} \pm s$)

Parameter	Groups	T_0	T_1	T_4	T_5
E/(ng/mL)	C(n=32)	34.13±5.22	55.94±6.98[1)]	62.34±6.91[1)]	58.59±7.21[1)]
	D(n=30)	32.83±7.78	41.83±7.79[1)2)]	51.20±6.84[1)2)]	46.27±7.01[1)2)]
	$F_{Groups/Factor/Factor\ interaction}$	33.45/911.08/73.23			
	$P_{Groups/Factor/Factor\ interaction}$	<0.001/<0.001/<0.001			
Cor/(mmol/L)	C(n=32)	177.47±14.46	228.75±15.60[1)]	241.88±20.07[1)]	233.81±21.52[1)]
	D(n=30)	186.63±21.95	203.53±24.36[1)2)]	221.23±26.06[1)2)]	214.23±25.91[1)2)]
	$F_{Groups/Factor/Factor\ interaction}$	7.21/579.99/74.65			
	$P_{Groups/Factor/Factor\ interaction}$	0.009/<0.001/<0.001			
Glu/(mmol/L)	C(n=32)	4.82±0.48	5.79±1.05[1)]	6.26±0.93[1)]	5.88±0.63[1)]
	D(n=30)	4.94±0.46	5.24±0.91[1)2)]	5.61±0.99[1)2)]	5.45±0.48[1)2)]
	$F_{Groups/Factor/Factor\ interaction}$	6.78/32.88/4.82			
	$P_{Groups/Factor/Factor\ interaction}$	0.012/<0.001/0.003			

Compare with T_1, [1)]P<0.05, Compare with Group C, [2)]P<0.05. E: epinephrine; Cor: cortisol; Glu: glucose

2.5 两组术后不良反应的比较

D组术后ED的发生率为16.67%,明显低于C组的40.63%(P=0.039);CRBD的发生率6.67%低于C组的28.13%(P=0.044);D组术后追加镇痛药的例数低于C组,术后嗜睡和恶心呕吐例数高于C组,但差异无统计学意义(P>0.05;表6)。

2.6 术后48 h新的适应不良行为比较

2组术后48 h内均有不同程度的新适应不良行为出现,表现为失眠、噩梦、发脾气、注意力缺乏、分离性焦虑等,单一表现组间差异无统计学意义。与C组相比,D组总的发生率较低(13.33% *vs.* 37.50%, P=0.042),合计频次较低(6人次 *vs.* 16人次, P=0.014),差异有统计学意义(P<0.05,表7)。

3 讨 论

ED是小儿全麻苏醒期常见的并发症,尽管已有大量的临床及基础研究,其发生机制仍不十分清楚[1,12]。隐匿性阴茎是阴茎体位于会阴部深处的一种先天性外生殖器畸形,外科矫治手术时间虽短,但因阴茎体神经丰富且反应敏感,手术可引起剧烈的疼痛[8-9]。在小儿隐匿性阴茎矫治术中,七氟烷吸入麻醉、术后常规留置导尿管的刺激及切口疼痛均是增加ED发生的高危因素[1-2]。临床研究表明围术期给予咪达唑仑、阿片类药物、右美托咪定等镇静镇痛药可以明显减少ED的发生率[1]。地佐辛是μ受体激动/拮抗剂、κ受体拮抗剂,副作用小,广泛用于临床辅助镇痛[4-6],本研究表明地佐辛超前

表6 两组术后不良反应的比较

Table 6 The comparison of postoperative adverse reactions between two groups [n(%)]

Groups	ED	CRBD	Additional analgesic	PONV	Drowsiness
C(n=32)	13(40.63)	9(28.13)	10(31.25)	2(6.25)	3(9.38)
D(n=30)	5(16.67)[1)]	2(6.67)[2)]	3(10.00)[2)]	3(10.00)[2)]	5(16.67)[2)]
χ^2	4.244	–	–	–	–
P	0.039	0.044	0.061	0.667	0.467

[1)]tested by Pearson Chi-Square, [2)] tested by Fisher's Exact Test. ED: emergence delirium, PONV: nausea and vomiting, CRBD: catheter-related bladder discomfort

表7　术后48 h新的适应不良行为比较

Table 7　Compare new maladaptive behaviors within 48 h after Operation　*n*(%)

New maladaptive behaviors	C(*n*=32)	D(*n*=30)	χ^2	*P*
Sleep disturbances	3(9.38)	1(3.33)[2)]	–	0.613
Nightmare	4(12.50)	2(6.67)[2)]	–	0.672
Temper tantrums	5(15.63)	1(3.33)[2)]	–	0.197
Attention seeking	2(6.25)	1(3.33)[2)]	–	1.000
Separation anxiety	1(3.12)	1(3.33)[2)]	–	1.000
Others	1(3.12)	0[2)]	–	1.000
Total Frequency (person-time)	16(50.00)	6(20)[1)]	5.989	0.014
Total cases	12(37.50)	4(13.33)[2)]	–	0.042

[1)] tested by Pearson Chi-Square, [2)] tested by Fisher's Exact Test.

镇痛可明显降低小儿隐匿性阴茎矫治术后PAED及FLACC评分，降低术后ED及CRBD发生率，且可降低术后6 h内的应激反应水平，降低术后2天内的新发适应不良行为的总发生率。

小儿术后ED的发生率25%～80%[12]，大部分ED事件发生在到达PACU后30 min内，ED具有自限性特点，但有部分患儿在术后一段时间内出现新的适应不良行为，表现失眠、噩梦、发脾气、注意力缺乏、分离性焦虑等[1]。本研究中虽两组均给予右美托咪定静脉输注及舒芬太尼联合DPNB镇痛[1-2]，C组术后ED的发生率仍高达40.63%，D组术后ED的发生率降为16.67%(*P*=0.039)；在T_2～T_5时间点，PAED评分均明显低于C组(*P*<0.001)，术后48 h内新发适应不良行为的总发生率明显低于C组(13.33% *vs.* 37.50%, *P*=0.042)；说明地佐辛超前镇痛可以明显降低小儿隐匿性阴茎术后ED及后继的新适应不良行为的发生率。

地佐辛具有与吗啡相同的镇痛作用[13]，能有效缓解中重度手术疼痛；可抑制5-羟色胺和去甲肾上腺素再吸收，降低纯μ阿片受体激动剂的不良反应[4-5]，在国内常与阿片类药物联合用于围术期镇痛[14-15]。因其消除半衰期约1.2～7.4 h[2]，故而超前镇痛后我们设计只观察术后6小时。结果表明D组在T_2～T_5点FLACC评分明显低于C组(*P*<0.001)；且D组在T_1、T_4、T_5时间点E、Cor、Glu值明显低于C组(*P*值分别为<0.001, 0.009, 0.012)，HR、MAP在T_2点波动幅度较小(*P*<0.05)；说明地佐辛超前镇痛明显降低术后6 h内疼痛评分，有助于减少术后镇痛药的用量，降低疼痛引起的相关应激反应水平。

外科导尿患者术后CRBD的发生率为47%～90%，CRBD增加术后疼痛和ED[2, 16-18]，右美托咪定[12,18-19]、镇痛药[17]、DPNB[19]均可明显改善CRBD的症状及降低其发生率。本研究中2组均给予DPNB及右美托咪定的前提下，D组CRBD的发生率明显低于C组(6.67% *vs.* 28.13%, *P*=0.044)，与Zhang等[2]研究结果一致，其机制可能与地佐辛拮抗κ阿片受体作用相关。D组术后嗜睡及恶心呕吐例数虽高于C组，但差异无统计学意义(*P*>0.05)，表明地佐辛在降低ED的同时，并不明显增加恶心呕吐、嗜睡等不良反应，亦是其作为非纯μ阿片受体激动剂药理特性的体现[4-6]。

综上所述，地佐辛超前镇痛可明显降低小儿隐匿性阴茎术后ED的发生率；降低术后新发适应性不良行为的发生率，可能与地佐辛降低术后疼痛应激及CRBD发生率有关。

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(编辑 余 菁)