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◇药物与临床◇

右美托咪定与利多卡因预处理对全麻诱导时依托咪酯不良反应的影响

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摘要: 目的 观察右美托咪定与利多卡因预处理对全身麻醉诱导期依托咪酯注射痛及肌阵挛的影响。**方法** 选择2018年6月至2019年6月河北工程大学附属医院择期手术全麻病人144例,ASA分级Ⅰ~Ⅱ,采用随机数字表法分为三组:对照组(C组)、右美托咪定组(D组)、利多卡因组(L组),每组48例。D组和L组病人分别预先泵注右美托咪定0.5 μg/kg和利多卡因1 mg/kg;C组给予等容量0.9%氯化钠溶液(10 mL),均在10 min注射完毕。然后各组病人静脉推注依托咪酯0.3 mg/kg,注射时间30 s。分别干预给药前(T_0)、给依托咪酯前(T_1)、及给依托咪酯后1 min(T_2)、2 min(T_3)记录病人HR(心率)、MAP(平均动脉压)、SpO_2(血氧饱和度)、镇静评分,并记录注射痛、低血压和心动过缓发生率,评估肌阵挛发生情况及严重程度。**结果** 与C组比较,D组和L组的肌阵挛发生率明显降低($P<0.05$);而D组与L组之间肌阵挛发生率及程度差异无统计学意义。D组镇静评分明显高于C组和L组($P<0.05$);与C组比较,D组和L组的注射痛发生率明显降低($P<0.05$);而D组与L组之间注射痛发生率差异无统计学意义。各组均无低血压和心动过缓发生。D组和L组MAP均在T_1(79.5±6.4)、T_2(74.8±5.8)、T_3(66.9±5.4) mmHg逐渐降低;C组和L组HR均在T_1(74.3±3.7)、T_2(79.0±3.5)、T_3(84.3±3.1)次/分钟逐渐升高;三组MAP和HR组间、时点间和组间×时点间交互作用均差异有统计学意义($P<0.05$)。三组SpO_2组间、时点间和交互作用均差异无统计学意义($P>0.05$)。

结论 右美托咪定与利多卡因预处理,均可减少麻醉诱导期依托咪酯所致的肌阵挛及注射痛的发生;与利多卡因相比,右美托咪定可提供更稳定的血流动力学。

关键词: 依托咪酯; 药物相关性副作用和不良反应; 麻醉,全身; 右美托咪定; 利多卡因; 肌阵挛; 注射痛

Effect of dexmedetomidine and lidocaine pretreatment on adverse reactions of etomidate during general anesthesia induction

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Abstract: Objective To observe the effect of dexmedetomidine and lidocaine pretreatment on injection pain and myoclonus of etomidate during general anesthesia induction.**Methods** From June 2018 to June 2019,144 patients (ASA Ⅰ ~ Ⅱ) had surgery during this period were randomly divided into3 groups (N=48):control group (Group C),Dex group (Group D),and lidocaine group (Group L)by random number table method.Patients in Group D and Group L received intravenous Dex 0.5 μg/kg and lidocaine 1 mg/kg respectively,while patients in group C received intravenous normal saline with the same volume (10 mL) within10 min.Then etomidate 0.3 mg/kg was injected intravenously for 30 s.Heart rate(HR),mean arterial pressure(MAP),oxygen saturation(SpO_2) and Ramsay score were recorded before drug (T_0),to etomidate before (T_1) and to 1 min(T_2),2 min(T_3) after etomidate.The adverse effects such as injection pain and adverse cardiovascular events were also recorded.The onset of myoclonus was observed and the severity was recorded.**Results** Compared with group C,the incidence of myoclonus in group D and group L was significantly lower ($P<0.05$),but there was no significant difference in the incidence and degree of myoclonus between group D and group L.Sendation score in Group D was significantly higher than the other two groups ($P<0.05$).Comparing to group C,the incidence of pain in Group C was significantly higher than that in Group L and Group D ($P<0.05$).The frequency of etomidate injection pain were statistically similar between Group L and Group D.No hypotension and bradycardia occurred in all groups.The groups D and groups L of MAP were gradually lower at T_1(79.5±6.4),T_2(74.8±5.8),T_3(66.9±5.4)mmHg time point;The groups C and groups L of HR were gradually higher at T_1(74.3±3.7),T_2(79.0±3.5),T_3(84.3±3.1)bpm time point.In MAP and HR,interblock、time dissimilarity and interaction of interblock with time dissimilarity of the three groups had statistically significant difference($P<0.05$).For SpO_2,there was no significant difference among the three groups ($P>0.05$).**Conclusion** Dexmedetomidine and lidocaine pretreatment can reduce etomidate induced myoclonus and injection pain during anesthesia induction;compared with lidocaine,pretreatment of dexmedetomidine can provide a more stable hemodynamics.

Key words: Etomidate; Drug-related side effects and adverse reactions; Anesthesia,general; Dexmedetomidine; Lidocaine; Myoclonus; Injection pain

依托咪酯属快速催眠全身静脉麻醉药,对心血管系统及呼吸系统的影响较小,血流动力学稳定,适用于老年或循环不稳定病人的全麻诱导[1-2]。但是依托咪酯在诱导过程中会引起一些副反应,诸如注射痛、肌阵挛等[3]。有研究显示静脉输注利多卡因[4]和右美托咪定[5](Dex)都可以有效抑制依托咪酯注射痛及肌阵挛,但两者之间是否存在差异,目前尚不清楚。本研究旨在比较静脉输注利多卡因与右美托咪定对麻醉诱导期依托咪酯不良反应的影响,为临床提供参考。

1 资料与方法

1.1 一般资料 选择河北工程大学附属医院2018年6月至2019年6月择期接受气管插管全身麻醉下手术的144例,均为ASA(美国麻醉医师协会分级)Ⅰ级~Ⅱ级;按照随机数字表法将病人分为右美托咪定组(D组)、利多卡因组(L组)和对照组(C组),各48例。排除标准:严重室内及房室传导阻滞,神经系统或精神疾病,肝肾功能不全以及近期服用镇静以及阿片类药物的病人,对本研究所使用的药物有过敏反应及禁忌证的病人。本研究符合《世界医学协会赫尔辛基宣言》相关要求。所有病人或其近亲属术前已签署知情同意书。

1.2 麻醉方法 病人术前常规禁饮、禁食,均未给予术前用药。病人入室后面罩吸氧5 L/min及建立前臂静脉通路,持续静脉滴注乳酸林格液,速率为10 mL·kg^{-1}·h^{-1}。使用飞利浦监护仪MP30常规监测心率(HR)、平均动脉压(MAP)、脉搏氧饱和度(SpO_2)、脑电双频指数(BIS)。麻醉诱导前,D组病人静脉泵注Dex(江苏恒瑞医药股份有限公司,批号181230BP,国药准字H20090248)0.5 μg/kg,L组病人静脉泵注利多

卡因1 mg/kg。Dex和利多卡因均以0.9%氯化钠溶液稀释至10 mL,用输注泵10 min注射完毕,C组病人则输注等量0.9%氯化钠溶液。1 min后静脉注射依托咪酯(江苏恩华药业股份有限公司,批号20180207,国药准字H20020511)0.3 mg/kg,注射时间30 s。90 s后均给予咪达唑仑0.05 mg/kg,舒芬太尼0.6 μg/kg以及顺苯磺酸阿曲库铵0.15 mg/kg全麻诱导,而后可视喉镜下插入气管导管,连接麻醉机,行机械通气,术中以静吸复合维持麻醉。麻醉手术期间所有病人未出现意外事件,手术顺利术毕安返病房。术后24 h回访,病人均未出现红疹、肿胀、疼痛及过敏反应等并发症,并且均未发生术中知晓。

1.3 观察指标 观察预给药前(T_0)、给依托咪酯前(T_1)及给依托咪酯后1 min(T_2)、2 min(T_3)记录病人的MAP、HR、SPO_2以及静注依托咪酯后2 min内肌阵挛发生情况,以及低血压(MAP降低超过基础值30%)、心动过缓(HR<50次/分)、注射痛发生率。肌阵挛定义:由于肌肉无意识短暂收缩引起肉眼可见的肢体动作。肌阵挛严重程度分级标准:0级为未见肢体动作,1级为轻度肌阵挛(肢体某一部分微小的运动,如手指或脚趾的收缩);2级为中度肌阵挛(两块不同的肌肉或肌群的运动,如手臂或腿);3级为重度肌阵挛(两块或更多的肌群收缩,如肢体的快速外展或屈曲)。依托咪酯引起肌阵挛多发生在静脉注射30~90 s[6],所以本研究持续观察120 s。各组病人在注射依托咪酯前进行Ramsay镇静评分[1]。

1.4 统计学方法 采用SPSS 16.0统计软件进行统计分析。计量资料采用$\bar{x}\pm s$表示,组间比较采用单因素方差分析及重复测量方差分析;计数资料比较采用χ^2检验;镇静评分以中位数及下、上四分位数表示,组间镇静评分比较采用秩和检验;以$P<0.05$为差异有统计学意义。

2 结果

2.1 一般情况比较 三组病人年龄、性别比、身高、体质量、ASA分级差异无统计学意义,见表1。

表1 依托咪酯全身静脉麻醉144例一般资料的比较

组别	例数	年龄/(岁,$\bar{x}\pm s$)	性别比(男/女)/例	身高/(cm,$\bar{x}\pm s$)	体质量/(kg,$\bar{x}\pm s$)	ASA分级(Ⅰ/Ⅱ)/例
C组	48	49.1±9.5	24/24	165±7	63.4±9.2	23/25
D组	48	41.5±8.4	25/23	164±9	64.1±11.3	24/24
L组	48	40.2±8.5	26/22	165±6	63.6±8.6	21/27
$F(\chi^2)$值		2.736	(0.167)	0.375	0.632	(0.390)
P值		0.097	0.920	0.709	0.538	0.832

2.2 三组肌阵挛的比较 与C组比较,D组和L组的肌阵挛发生率明显降低($P<0.05$);而D组与L组之间肌阵挛发生率及程度差异无统计学意义。见表2。

表2 依托咪酯全身静脉麻醉下144例肌阵挛发生情况/例(%)

组别	例数	0级	1级	2级	3级	合计
C组	48	12(25.00)	10(20.83)	15(31.25)	11(22.92)	36(75.00)
D组	48	47(97.92)	1(2.08)	0(0)	0(0)	1(2.08)①
L组	48	46(95.83)	1(2.08)	1(2.08)	0(0)	2(4.17)②③

注:三组依托咪酯用药后肌阵挛程度及发生率比较,$U=89.536$,$P<0.001$;$\chi^2=75.836$,$P<0.001$。

①与C组比较,$\chi^2=53.871$,$P<0.001$。②与C组比较,$\chi^2=50.352$,$P<0.001$。③与D组比较,$\chi^2=0.344$,$P=0.558$。

2.3 三组镇静评分及低血压、心动过缓、注射痛发生率比较 D组镇静评分明显高于N组和L组($P<0.05$);与C组比较,D组和L组的注射痛发生率明显降低($P<0.05$);而D组与L组之间注射痛发生率差异无统计学意义。各组均无低血压和心动过缓发生。见表3。

表3 依托咪酯全身静脉麻醉144例镇静评分及注射痛发生率比较

组别	例数	Ramsay评分/$M(P_{25},P_{75})$	注射痛/例%
C组	48	2(1,2)①	8(16.67)
D组	48	3(1,4)	1(2.08)②
L组	48	2(1,2)①	2(4.17)②
$U(\chi^2)$值		21.600	(6.405)
P值		0.008	0.011

注:①与D组比较,$U=18.500$、$P=0.015$,$U=17.500$、$P=0.011$。②与C组比较,$\chi^2=6.008$、$P=0.014$,$\chi^2=4.019$、$P=0.045$。

2.4 三组血流动力学比较 D组和L组MAP均在T_1~T_3逐渐降低;C组和L组HR均在T_1~T_3逐渐升高;三组MAP和HR组间、时间和交互均差异有统计学意义($P<0.05$)。三组SpO_2组间、时间和交互均差异无统计学意义($P>0.05$)。见表4。

表4 依托咪酯全身静脉麻醉144例血流动力学比较/$\bar{x}\pm s$

组别	例数	HR/(次/分)	MAP/mmHg	SPO_2/%
C组	48			
T_0		73.4±4.5	96.4±12.6	99.4±0.4
T_1		74.3±3.7	95.7±15.1	99.4±0.3
T_2		79.0±3.5	88.9±11.5	98.7±0.5
T_3		84.3±3.1	79.8±12.2	98.8±0.4
D组	48			
T_0		78.1±9.1	96.2±13.6	99.5±0.3
T_1		60.5±4.1	79.5±6.4	99.1±0.5
T_2		60.0±3.1	74.8±5.8	98.9±0.5
T_3		59.6±3.5	66.9±5.4	98.1±0.9
L组	48			
T_0		81.7±12.0	94.7±14.0	99.2±0.3
T_1		67.3±6.2	85.0±10.3	99.5±0.4
T_2		72.8±5.2	76.9±7.0	98.8±0.4
T_3		76.6±5.4	69.7±5.1	98.4±0.7
时间 F,P 值		6.566,0.031	5.401,0.045	1.235,0.336
组间 F,P 值		11.029,0.009	8.218,0.019	1.059,0.330
交互 F,P 值		5.070,0.034	6.521,0.031	1.412,0.265

3 讨论

依托咪酯注射痛可能源于依托咪酯直接刺激粘膜和静脉管壁引起[1];而肌阵挛的发生机制尚不完全清楚,有研究认为依托咪酯通过影响γ-氨基丁酸A型受体来抑制脑干网状结构的功能,使支配骨骼肌通路的敏感性增强,导致自发神经冲动发生,引起肌阵挛[7]。还有研究认为依托咪酯能与脑内多巴胺受体相结合,抑制其生物学功能,表现出多巴胺不足的临床表现,即肌阵挛[8]。

为减少依托咪酯诱导时所致的注射痛和肌阵挛,目前存在大量的研究及方法,主要包括诱导前静脉预注阿片类药物、利多卡因、苯二氮卓类药物、羟考酮等[9-14],但尚无统一标准。

本研究发现对照组依托咪酯引起的注射痛及肌阵挛发生率和已有报道相近[1,5]。已有研究表明[15-17] Dex定0.2~0.5 μg/kg,既能产生较好的镇静镇痛作用,又极少对血压、心率产生副反应;由于静脉快速大量输注Dex定可能引起血流动力学的不稳定,因此本研究Dex定剂量选择0.5 μg/kg,并采用静脉泵注10 min的方式注射药物。同时,这种注射方式也可延长利多卡因与注射部位血管壁接触时间,既加强局部静脉麻醉作用,也减少了大量使用利多卡因对心脏产生的副作用。本研究结果表明,诱导前预先泵注Dex定0.5 μg/kg及利多卡因1 mg/kg均能明显降低依托咪酯引起的注射痛及肌阵挛的发生率。

Dex降低全麻诱导期依托咪酯注射痛及肌阵挛的发生,可能是由于其激动中枢α_2肾上腺素受体,抑制交感神经过度兴奋,减少血液中儿茶酚胺的释放,减轻了病人术前的应激反应所致。利多卡因减轻肌阵挛的机制可能是由于其本身加强了中枢镇静,且抑制引发肌阵挛的神经中枢部位,减轻了肌阵挛过程中的炎症反应与应激反应[4,18]。

本研究结果表明Dex 0.5 μg/kg和利多卡因1 mg/kg对减轻注射痛及肌阵挛效果相当,但麻醉诱导前D组镇静评分明显高于L组和C组,因而Dex还具有镇静及抑制交感活性作用。本研究中右美托咪定与依托咪酯合用,可明显抑制反射性心率增快,呼吸抑制轻,还减少术中全麻药用量,减轻术后躁动谵妄及恶心呕吐[19]。因此与利多卡因相比,Dex 0.5 μg/kg预处理,不仅能减少麻醉诱导期依托咪酯所致注射痛及肌阵挛的发生率,还可提供更稳定的血流动力学。

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