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不同剂量右美托嘧啶对胸腔镜下食管癌根治术患者心肌氧供及血流动力学的影响

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摘要 目的：探讨不同剂量右美托嘧啶(DEX)对胸腔镜下食管癌根治术患者心肌氧供及血流动力学的影响。**方法：**选取 66 例我院拟行腔镜下食管癌根治术患者，随机分为三组，每组各 22 例：低剂量右美托嘧啶组（L 组）(0.5 μg/kg)、高剂量右美托嘧啶组（H 组）(1.0 μg/kg)、对照组（N 组）(与 L 组和 H 组同等速率输注生理盐水)，而后 H 组和 L 组均以 0.5 μg/kg/h 维持输注 DEX。记录各组输注前（T1）、输注后 5 min（T2）、输注后 10 min（T3）、输注后 15 min（T4）、输注后 30 min（T5）各组血流动力学指标：心率（HR）、收缩压（SBP）、平均动脉压（MAP）、每搏输出量（SV）、中心静脉压（CVP）、心排量（CO），计算 HR 与 SBP 的乘积 RPP，抽取挠动脉和肺动脉血进行动脉血气分析，采用反向 FICK 法计算氧供（DO_2）和氧耗（VO_2）。**结果：**HR：H 组和 L 组患者 HR 随时间的推移呈下降趋势，H 组 T3、T4、T5 时间点 HR 较 T1 时间点显著降低（P<0.05）；与 N 组相比，H 组和 L 组 T3、T4、T5 时间点 HR 显著降低（P<0.05）。MAP：H 组 T3、T4、T5 时间点 MAP 显著低于 L 组（P<0.05）；H 组 T3、T4 时间点 MAP 显著低于 N 组（P<0.05）；H 组 T5 时间点 MAP 显著低于同组 T1、T2 时间点（P<0.05）。SBP：H 组 T3、T4、T5 时间点 SBP 与 L 组和 N 组比较显著降低（P<0.05）；H 组 T5 时间点 SBP 较同组 T1、T2 时间点显著降低（P<0.05）。RPP：H 组 T3、T4、T5 时间点 RPP 与同组 T1、T2 时间点和 N 组比较显著降低（P<0.05）。DO_2：H 组 T5 时间点 DO_2 与 L 组和 N 组比较显著降低（P<0.05）。VO_2：L 组患者 VO_2 T3、T4、T5 时间点与组内 T1、T2 时间点和 N 组相比显著降低（P<0.05）；H 组 VO_2 T3、T4、T5 时间点与组内 T1、T2 时间点和 N 组相比显著降低（P<0.05）。**结论：**小剂量（0.5 μg/kg）输注 DEX 能降低胸腔镜下食管癌患者心肌氧耗，维持血流动力学稳定，高剂量（1.0 μg/kg）输注 DEX 降低心肌氧耗的同时会降低心肌氧供，存在一定风险，对于患有冠心病以及心肺功能低下的老年患者，建议给予小剂量输注 DEX，并监测血流动力学指标，及时调整 DEX 用量。

关键词：右美托嘧啶；剂量；食管癌根治术患者；心肌氧供；血流动力学

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The Effects of Dexmedetomidine of Two Different Dose Infusion on Myocardial Oxygen Supply and Hemodynamics in Patients with Radical Resection of Esophageal Carcinoma under Thoracoscopy Surgery

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ABSTRACT Objective: To explore the effects of dexmedetomidine of two different dose infusion on myocardial oxygen supply and hemodynamics in patients with radical resection of esophageal carcinoma under thoracoscopy surgery. **Methods:** 66 cases with radical resection of esophageal carcinoma under thoracoscopy surgery in our hospital were enrolled in the study. These patients were randomly divided into three groups, there were 22 people in each group: Low dose dexmedetomidine group (Group L)(0.5 μg/kg), High dose dexmedetomidine group(Group H)(1.0 μg/kg) and Normal saline(Group N)(infusing physiological saline at the same rate of Group L and Group H). Then the same rate of maintecance infusing DEX of group H and L was 0.5 μg/kg/h. Hemodynamic index incloding: HR, SBP,MAP, SV, CVP, CO, HR× SBP (RPP), pulmonary blood gas analysis, oxygen supply (DO_2)and oxygen consumption (VO_2) at five time points were recorded: before DEX and physiological saline infusion (T1), infusion 5 min later (T2), DEX and infusion 10 min later (T3), infusion 15 min later(T4), infusion 30 min later(T5). **Results:** HR of group H and L patients showed up a depression trend; In Group

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H, compared with T1 time point, HR of T3, T4 and T5 time points reduced significantly (P<0.05); Compared with Group N, HR of the group H and L T3,T4 and T5 time points reduced significantly (P<0.05). Compared with Group L, MAP of group H T3, T4 and T5 time points reduced significantly (P<0.05); Compared with Group N, MAP of the group H T3, T4 and T5 time points reduced significantly (P<0.05); Compared with T1, T2 time points in Group H, MAP of T5 time points reduced significantly (P<0.05) Compared with Group L and Group N, SBP of group H T3, T4 and T5 time points reduced significantly (P<0.05); Compared with T1, T2 points in Group H, SBP of T5 time points reduced significantly (P<0.05); Compared with T1,T2 time points in Group H and Group N, RPP of T3, T4, T5 time points in Group H reduced significantly (P<0.05). Compared with Group L and Group N, DO_2 of T5 time points in Group H reduced significantly (P<0.05); Compared with T1, T2 time points in Group L and Group N, VO_2 of T3, T4, T5 time points in Group L reduced significantly (P<0.05); Compared with T1, T2 time points in Group H and Group N, VO_2 of T3, T4, T5 time points in Group H reduced significantly (P<0.05). **Conclusion:** Low dose DEX infusion (0.5 μg/kg) could reduce myocardial oxygen consumption of patients with radical resection of esophageal carcinoma under thoracoscopy surgery and maintain hemodynamic stability, high dose DEX infusion (1.0 μg/kg) could reduce myocardial oxygen consumption, which could reduced myocardial oxygen supply at the same time, there is a risk. For elderly patients with coronary heart disease and low cardiopulmonary function, low doses DEX infusion was suggested, and monitoring hemodynamic parameters, adjust the dose of DEX timely.

Key words: Dexmedetomidine; Dose; Patients with radical resection of esophageal carcinoma under thoracosocopy surgery; Myocardial oxygen supply; Hemodynamics

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前言

食管癌是全球常见癌症,高居癌症死亡原因的第六位[1]。手术治疗是食管癌的首选治疗方法,以往多采取开胸手术,但存在术中出血量多、手术时间长、术后并发症多等缺点,随着胸腔镜技术的发展与完善,以其创伤小、恢复快、术野清晰等优点,逐渐取代了传统开胸术[2,3]。右美托嘧啶(dexmedetomidine,DEX)作为a2肾上腺素受体激动剂,被应用于围术期,能改善心肌氧供需平衡和维持血流动力学稳定[4]。食管癌患者多为老年患者,各脏器功能减退,常合并心肺系统疾病,在术中应用右美托嘧啶,对降低其手术风险、减少术后并发症的发生有着重要的意义[5,6]。有研究发现[7],不同剂量右美托嘧啶对术中血流动力学的影响存在差异,本文通过研究不同剂量DEX对胸腔镜下食管癌根治术患者心肌氧供及血流动力学的影响,探讨术中应用DEX的最佳剂量。现报道如下:

1 资料与方法

1.1 临床资料

选取2015年9月-2016年2月我院拟行腔镜下食管癌根治术的患者66例。纳入标准:⑴ 年龄60-70岁;⑵ 术前病理检查明确诊断为食管癌;⑶ 美国麻醉医师协会(American Society of Anesthesiologists,ASA)分级为Ⅱ级。排除标准:⑴ 合并严重心、肝、肺、肾等重要脏器疾病者;⑵ 患有严重内分泌、神经系统疾病者;⑶ 患有精神类疾病者;⑷ 近期服用镇静催眠药物者;⑸ 对本研究药物过敏者。采用随机数字法将66例患者随机分为三组:低剂量DEX组(L组)、高剂量DEX组(H组)、对照组(N组),每组各22人。三组患者年龄、性别、身高、体重等一般情况比较,差异无统计学意义(P>0.05),具有可比性,见表1。试验过程经伦理委员会通过,且所有患者均签署知情同意书。

表1 三组患者一般情况比较(n=22,$\bar{x}\pm s$)

Table 1 Comparision of general condition of the three groups(n=22,$\bar{x}\pm s$)

Groups	Gender(M/F)	Aage(years)	Height(cm)	Wweight(kg)	BMI(kg/m²)
Group L	10/12	67.34± 3.23	167.07± 8.55	65.39± 14.22	25.19± 4.17
Group H	13/9	68.92± 3.74	165.33± 7.92	67.21± 13.24	26.27± 3.97
Group N	12/10	68.13± 2.98	165.35± 8.38	65.92± 12.78	25.83± 4.28
F	2.122	2.109	2.119	2.053	1.974
P	0.073	0.078	0.075	0.081	0.085

1.2 研究方法

各组术前给予常规禁食禁水,入室后按常规监测无创血压、血氧饱和度、心电图变化。进入手术室后开放静脉通路,各组均给予5-10 mL/kg/h林格氏液。诱导麻醉前15 min,给予H组输注DEX剂量为1.0 μg/kg(江苏恒瑞医药股份有限公司,H20090248,规格为2 mL),L组输注DEX剂量为0.5 μg/kg,分别加入生理盐水中配成50 mL溶液,在输液泵的控制下,15min内输完,N组以同等速率输注生理盐水。而后H组、L组继续以0.5 μg/kg/h输注DEX,N组以同等速率输注生理盐水。研究安全控制:输注DEX期间,心率低于50次/min以下者,给予每

次静脉输注阿托品 0.5 mg 治疗；血压低于基础值 25%时，及时补充血容量并调整麻醉药物剂量后仍未缓解，给予静脉输注麻黄碱 10 mg 治疗。

1.3 监测指标

采用 USCOM 无创血流动力学监测仪，记录各组输注前（T1）、输注后 5 min（T2）、输注后 10 min（T3）、输注后 15 min（T4）、输注 30 min（T5）血流动力学指标，包括心率（heart rate, HR）、收缩压（systolic blood pressure,SBP）平均动脉压（mean arterial pressure, MAP），每搏输出量（stroke volume,SV）、中心静脉压（central venous pressure, CVP）、心排量（cardiac output, CO），计算 HR 与 SBP 的乘积(HR× SBP, RPP)，抽取挠动脉和肺动脉血进行动脉血气分析，采用反向 FICK 法计算氧供（oxygen delivery，DO_2）和氧耗（oxygen consumption，VO_2）。

1.4 统计学处理

采用 SPSS 19.0 统计软件进行数据分析，计量资料以均数± 标准差（$\bar{x}$± s）表示，各组患者一般情况比较采用卡方检验，组内比较重复测量的方差分析，组间比较采用成组 t 检验。

2 结果

2.1 三组患者血流动力学比较

HR：H 组和 L 组患者 HR 随时间的推移呈下降趋势(P<0.05)，H 组 T3、T4、T5 时间点较 T1 时间点显著降低（P<0.05）；与 N 组相比，H 组和 L 组 T3、T4、T5 时间点显著降低（P<0.05）。MAP：H 组 T3、T4、T5 时间点 MAP 显著低于 L 组（P<0.05）；H 组 T3、T4 时间点 MAP 显著低于 N 组（P<0.05）；H 组 T5 时间点 MAP 显著低于同组 T1、T2 时间点（P<0.05）。SBP：H 组 T3、T4、T5 时间点 SBP 与 L 组和 N 组比较显著降低（P<0.05）；H 组 T5 时间点 SBP 较同组 T1、T2 时间点显著降低 (P<0.05)。RPP：H 组 T3、T4、T5 时间点 RPP 与同组 T1、T2 时间点比较显著降低(P<0.05)，和 N 组比较显著降低（P<0.05）。H 组与 L 组 HR、RPP 比较，无显著差异（P>0.05）；L 组患者 MAP、SBP、RPP 不同时间点无显著变化（P>0.05）。见表 2。

表 2 三组患者血流动力学情况的比较

Table 2 Comparision of hemodynamics change of the three groups

Groups	Indexes	T1	T2	T3	T4	T5
Group L		75.32± 9.35	73.58± 10.48	59.23± 12.23^{b}	55.83± 11.25^{b}	52.57± 10.87^{b}
Group H	HR（min）	74.81± 10.43	71.65± 10.38	60.34± 9.32^{bd}	54.23± 10.35^{bd}	52.87± 12.09^{bd}
Group N		73.20± 9.98	73.06± 11.20	71.92± 11.45	70.26± 12.39	70.92± 11.75
Group L		143.54± 16.33	147.29± 13.93	143.31± 14.72	137.77± 12.22	133.98± 15.90
Group H	MAP（mmHg）	144.12± 15.43	136.23± 16.77	89.44± 16.09^{ad}	84.21± 11.34^{ad}	71.33± 14.54^{abc}
Group N		141.22± 14.88	143.23± 13.90	144.37± 14.81	143.29± 15.60	143.77± 15.26
Group L		128.77± 23.86	123.61± 26.17	124.55± 27.06	119.56± 23.21	118.87± 21.77
Group H	SBP(mmHg)	125.91± 22.98	121.44± 18.35	98.33± 16.44a^{d}	96.23± 23.32^{ad}	92.23± 15.45^{abcd}
Group N		127.33± 28.11	125.77± 27.55	131.88± 22.61	129.78± 21.74	122.44± 27.88
Group L		10198.23± 203.34	10104.94± 194.63	8943.28± 185.49	8947.92± 198.38	8623.27± 185.74
Group H	RPP	10221.34± 199.68	10210.45± 231.88	7439.94± 204.77^{bcd}	6734.44± 176.38^{bcd}	5944.45± 143.49^{bcd}
Group N		10163.91± 210.44	10139.40± 255.25	10159.94± 221.13	10153.77± 111.64	10145.88± 176.89
Group L		4.92± 1.34	4.30± 1.20	3.96± 1.24	3.86± 2.21	3.79± 1.79
Group H	CO(L/min)	4.87± 1.55	4.44± 2.12	4.01± 1.22	3.65± 1.78	3.82± 1.52
Group N		4.82± 1.22	4.81± 1.07	4.86± 1.21	4.85± 1.07	4.83± 1.33
Group L		4.55± 1.23	4.12± 1.53	3.92± 1.54	4.03± 1.45	4.12± 1.22
Group H	CVP(cmH_2O)	4.44± 1.18	4.3± 1.22	3.87± 2.10	3.66± 1.22	3.90± 1.41
Group N		4.38± 1.52	4.22± 1.51	4.51± 1.47	4.52± 1.52	4.61± 1.58
Group L		70.19± 7.38	73.22± 4.32	75.44± 6.66	74.35± 4.56	73.77± 4.87
Group H	SV(mL)	69.32± 6.68	62.33± 4.66	59.22± 4.87	54.23± 4.29	53.36± 5.89
Group N		71.30± 5.32	74.32± 4.19	75.22± 3.29	74.29± 5.58	74.22± 3.56
Group L		913.34± 53.29	908.55± 53.87	903.19± 50.81	896.41± 42.49	872.66± 42.33
Group H	DO_2 ($mL/min*m^2$)	903.89± 48.49	894.22± 54.64	854.23± 58.33	732.11± 54.77	621.09± 56.20^{ad}
Group N		906.33± 48.34	905.28± 58.33	904.39± 43.34	902.55± 43.90	904.44± 56.32
Group L		203.43± 51.33	187.23± 55.65	103.19± 43.83^{bcd}	98.12± 47.43^{bcd}	85.32± 43.19^{bcd}
Group H	VO_2 ($mL/min*m^2$)	205.34± 45.88	184.33± 48.40	103.31± 43.56^{bcd}	95.77± 46.54^{bcd}	85.43± 40.49^{bcd}
Group N		204.30± 53.46	203.56± 54.09	205.35± 58.32	205.12± 56.99	204.78± 53.21

Note: ^{a}P<0.05, Compare with Group L; ^{b}P<0.05, Compare with T1 in the same group; ^{c}P<0.05, Compare with T2 in the same group; ^{d}P<0.05, Compare with Group N.

2.2 三组患者心肌氧供需变化情况的比较

VO_2:L 组患者 VO_2 T3、T4、T5 时间点与组内 T1、T2 时间点相比显著降低(P<0.05),和 N 组相比显著降低(P<0.05);H 组 VO_2 T3、T4、T5 时间点与组内 T1、T2 时间点相比显著降低(P<0.05),和 N 组相比显著降低(P<0.05),差异有统计学意义。DO_2:H 组 T5 时间点 DO_2 与 L 组和 N 组比较显著降低(P<0.05)。H 组与 L 组 VO_2 比较,无显著差异(P>0.05);L 组患者 DO_2 不同时间点无显著变化(P>0.05)。见表 2。

3 讨论

心肌的氧供与心肌的血液供应、动脉血氧含量等密切相关。心肌的血液供应主要取决于患者的冠脉系统以及灌注压,动脉血氧含量与血氧饱和度、血红蛋白浓度等有关[8]。食管癌患者多为老年患者,其各脏器功能衰退,心肺功能减低,其中许多患者合并有冠心病等疾病。冠心病患者本身就会导致心肌氧供需失衡,加之心肺功能低下,动脉血氧含量减低,导致心肌氧供和氧耗失衡,心肌氧供降低而氧耗增加,心肌处于无氧代谢状态而导致心肌损害,甚至发生严重的并发症危及生命[9-12]。在心肌氧供和氧耗平衡关系中,心率是重要的观察指标。心率增加可使氧供降低的同时使氧耗增加。心率与收缩压的乘积 RPP 是临床常用的一项简便的反映心肌氧供和氧耗平衡与否的重要指标,正常值应低于 12 000。因此对于胸腔镜下食管癌根治术患者,在手术中应保持适当的冠状动脉的灌注压,保证心肌供血,提高氧供,同时使心率降低,减少心肌氧耗,维持血流动力学稳定。

在临床上最早使用的 a2 受体激动剂是可乐定,其应用领域十分广泛,有镇痛、降压、维持血流动力学平衡等作用,在临床中的应用越来越得到关注[13,14]。DEX 是一种新型的高选择性的亲脂性的 a2 肾上腺素能受体激动剂,与 a2 肾上腺素能受体的亲和力远高于可乐定,它能迅速分布到组织,药物起效快,药效持续时间长,且能维持血流动力学和循环系统功能稳定[15-17]。DEX 用作镇静剂应用于重症监护,被认为能够替代传统使用咪达唑仑和丙泊酚。与其他镇静剂相比,DEX 不抑制呼吸[18],对患者认知功能的影响优于异丙酚,有更好的麻醉唤醒作用,能更早拔管[19],目前已被逐渐广泛应用于手术患者[20]。

本研究结果显示,H 组和 L 组 T3、T4、T5 时间点 HR、RPP 与 N 组相比显著降低,L 组 VO_2T3、T4、T5 时间点与组内 T1、T2 时间点和 N 组相比显著降低;H 组 VO_2T3、T4、T5 时间点与组内 T1、T2 时间点和 N 组相比显著降低。说明高剂量输注 DEX 与低剂量输注 DEX 均能降低心率,减少心肌氧耗。但 H 组 T3、T4、T5 时间点 MAP 显著低于 L 组;H 组 T3、T4 时间点 MAP 显著低于 N 组;H 组 T5 时间点 DO_2 与 L 组和 N 组比较显著降低,提示高剂量输注 DEX 在降低心率减少氧耗的同时,会降低平均动脉压,影响冠状动脉灌注压力,使氧供降低。另外 H 组和 L 组 SV、CVP、CO 与 N 组相比,差异无统计学意义,提示高、低剂量 DEX 均对 SV、CVP、CO 无明显影响。右美托咪定具有较强的中枢性抗交感神经兴奋作用,同时还具有降低交感神经张力、镇痛等作用,从而保护心、脑等重要脏器[21,22]。但高剂量输注 DEX 在降低氧耗的同时,出现氧供的降低,无法确切评估其对心肌氧供需平衡的影响。

综上所述,小剂量(0.5 μg/kg)输注 DEX 能降低胸腔镜下食管癌患者心肌氧耗,维持血流动力学稳定,高剂量(1.0 μg/kg)输注 DEX 降低心肌氧耗的同时会降低心肌氧供,存在一定风险,对于患有冠心病以及心肺功能低下的老年患者,建议给予小剂量(0.5 μg/kg)输注 DEX,并监测血流动力学指标,及时调整 DEX 用量。

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