·论著·

持续输注超低剂量右美托咪定对老年CAS患者血流动力学和术后认知功能的影响

王晓宁[1],张丽红[2],张彤[3],李天佐[1]
(1. 首都医科大学附属北京世纪坛医院麻醉科,北京 100038; 2. 中国医科大学附属盛京医院麻醉科,沈阳 110004; 3. 首都医科大学附属北京世纪坛医院神经内科,北京 100038)

摘要 目的 探讨持续输注超低剂量右美托咪定对行颈动脉支架置入术(CAS)的老年患者血流动力学稳定性和术后认知功能的影响。**方法** 选取106例于首都医科大学附属北京世纪坛医院择期行CAS的老年患者,随机分为右美托咪定组(D组,$n=52$)和对照组(C组,$n=54$)。观察2组患者麻醉诱导前15 min(T0)、麻醉诱导后5 min(T1)、置入支架前5 min(T2)、置入支架后5 min(T3)、气管拔管后5 min(T4)的血流动力学和脑灌注变化;计算平均动脉压(MAP)、心率(HR)和脑氧饱和度(rSO_2)的标准差(SD),分别记作SD_{MAP}、SD_{HR}和SD_{rSO_2}。应用蒙特利尔认知评估量表(MoCA)对患者进行认知功能评估,比较患者术前、术后认知功能的变化,评价2组患者术后认知功能障碍(POCD)的发生情况。**结果** D组患者SD_{MAP}、SD_{HR}和SD_{rSO_2}均明显低于C组($P<0.05$);D组麻醉药及血管活性药使用量明显低于C组($P<0.05$);D组拔管时间明显短于C组($P<0.05$);D组术后1 d MoCA评分明显高于C组,术后30 d POCD发生率明显低于C组($P<0.05$)。**结论** 持续输注超低剂量右美托咪定可维持血流动力学和脑灌注稳定,减少麻醉药物用量,促进术后认知功能恢复。

关键词 右美托咪定;颈动脉支架置入术;血流动力学;术后认知功能障碍
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Effects of continuous infusion of extremely low-dose dexmedetomidine on the hemodynamic stability and postoperative neurological function of older adult patients undergoing CAS

WANG Xiaoning[1], ZHANG Lihong[2], ZHANG Tong[3], LI Tianzuo[1]
(1. Department of Anesthesiology, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China; 2. Department of Anesthesiology, Shengjing Hospital of China Medical University, Shenyang 110004, China; 3. Department of Neurology, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China)

Abstract Objective To investigate the effects of continuous infusion of extremely low-dose dexmedetomidine on the hemodynamic stability and recovery of postoperative cognition of older adult patients undergoing carotid artery stenting (CAS). **Methods** 106 older adult patients undergoing CAS were randomly divided into the dexmedetomidine (group D, $n=52$) and control groups (group C, $n=54$). Hemodynamic and cerebral perfusion changes were recorded 15 min before anesthesia induction (T0), 5 min after anesthesia induction (T1), 5 min before stent placement (T2), 5 min after stent placement (T3), and 5 min after tracheal extubation (T4). The standard deviations (SD) of mean arterial pressure (MAP), heart rate (HR), and regional cerebral oxygen saturation (rSO_2) were calculated as SD_{MAP}, SD_{HR}, and SD_{rSO_2}, respectively. The Montreal Cognitive Assessment Scale (MoCA) was used to evaluate and compare changes in pre- and postoperative cognitive function and examine the incidence of postoperative cognitive dysfunction (POCD) in the two groups. **Results** SD_{MAP}, SD_{HR}, and SD_{rSO_2} in group D were significantly lower than those in group C ($P<0.05$). The applied dosages of anesthetics and vasoactive drugs were significantly lower in group D than C ($P<0.05$). Extubation time in group D was significantly shorter than that in group C ($P<0.05$). MoCA scores in group D were significantly higher one day after CAS than that in group C and POCD incidence was significantly lower in group D one month after CAS ($P<0.05$). **Conclusion** Continuous infusion of low-dose dexmedetomidine has the potential to maintain hemodynamic stability and cerebral perfusion, reduce the dosage of anesthetic drugs, and improve postoperative cognitive performance in older adult patients.

Keywords dexmedetomidine; carotid artery stenting; hemodynamics; postoperative cognitive dysfunction

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作者简介:王晓宁(1978-),女,副主任医师,博士.
通信作者:李天佐,E-mail:ltzmzksss@126.com
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颈动脉狭窄是与缺血性卒中、认知障碍相关的老年常见疾病[1]。颈动脉支架置入术（carotid artery stenting，CAS）用于缓解老年患者的颈动脉狭窄，具有微创、安全的优点[2]。但严重的围手术期血流动力学波动和术后认知功能障碍（postoperative cognitive dysfunction，POCD）是CAS的主要风险[3]，影响患者的远期恢复。

右美托咪定是一种高选择性α2-肾上腺素能受体激动剂，能够稳定循环、减少拔管反应、提高麻醉恢复质量[4-5]，并显著降低神经损伤后的神经炎症和退行性变，减少脑缺血性损伤，改善并缩短POCD的持续时间[6]。常规推荐剂量使用右美托咪定可能导致老年患者出现剂量依赖性的血流动力学不稳定[4,6]。对于接受CAS的老年患者，超低剂量右美托咪定对血流动力学稳定性和术后认知功能的影响尚未确定。本研究旨在探讨持续静脉输注超低剂量右美托咪定对行CAS老年患者的血流动力学和术后认知功能的影响。

1　材料与方法

1.1　一般资料

选取2021年12月9日至2022年12月16日于首都医科大学附属北京世纪坛医院择期全身麻醉下行CAS的老年无症状颈动脉狭窄患者106例。纳入标准：（1）无症状单侧颈动脉狭窄>70%（严重狭窄），对侧颈动脉狭窄<30%；（2）完成认知功能测试；（3）美国麻醉医师协会分级（American society of anesthesiologists，ASA）Ⅱ～Ⅲ级；（4）年龄≥65岁。排除标准：（1）术前有精神病史或近期服用过精神药物；（2）严重心血管疾病，如房颤、心功能不全、严重心脏瓣膜病或严重心律失常等；（3）严重肺疾病或者呼吸功能不全；（4）严重肝脏、肾脏功能不全；（5）中度或重度贫血；（6）有酗酒史。将患者随机分为右美托咪定组（D组，n = 52）和对照组（C组，n = 54）。记录2组患者的一般情况，包括年龄、性别、身高、体质量、合并症、吸烟史等。本研究经北京世纪坛医院伦理委员会批准，患者均签署知情同意书。

1.2　麻醉方法

患者入室后进行心电监护，测量脉搏血氧饱和度、无创血压、脑电双频指数（bispectral index，BIS）和鼻温，采用局部脑氧饱和度（regional cerebral oxy-gen saturation，rSO_2）进行脑灌注监测。在麻醉诱导前，D组给予右美托咪定0.2~0.5 μg/kg（浓度4 μg/mL），10~15 min内静脉泵入，麻醉诱导后以0.1~0.2 μg/（kg·h）的剂量持续输注至手术结束前30 min；C组不给予右美托咪定，以相同速度泵入等量的生理盐水。2组的麻醉诱导均采用舒芬太尼1~2 μg/kg、丙泊酚1.5~2.5 mg/kg、罗库溴铵0.6~0.9 mg/kg。药物充分起效后进行气管内插管，机械通气，氧气流量2 L/min，潮气量8~10 mL/kg，呼吸频率12 次/min，吸呼比1 ∶ 2，维持呼气末二氧化碳分压35~45 mmHg。麻醉维持2组均采用瑞芬太尼和丙泊酚全凭静脉麻醉，维持BIS 40~60，体温36~37 ℃，间歇性给予罗库溴铵以维持肌肉松弛。手术结束待呼吸功能恢复后拔出气管插管，并将患者转运至麻醉后监测治疗室（postanesthesia care unit，PACU）。当患者Aldrete评分达到9分时由PACU转运至病房，记录患者在PACU的停留时间。

1.3　观察指标

记录麻醉诱导前15 min（T0）、麻醉诱导后5 min（T1）、置入支架前5 min（T2）、置入支架后5 min（T3）、气管拔管后5 min（T4）患者的平均动脉压（mean arterial pressure，MAP）、心率（heart rate，HR）和rSO_2。根据外科手术的要求，在动脉影像探查和置入支架的整个过程中，MAP维持<90 mmHg。当MAP < 60 mmHg或>110 mmHg时，给予去甲肾上腺素或乌拉地尔血管活性药物；当心率<45次/min或>90次/min时，静脉注射阿托品或艾司洛尔以维持血流动力学稳定。

计算每位患者T0~T4期间MAP、HR和rSO_2的标准差，以SD_{MAP}、SD_{HR}和SD_{rSO_2}表示，用于反映各指标的波动情况。采用蒙特利尔认知评估量表（montreal cognitive assessment，MoCA）对患者进行认知功能评估，记录所有患者术前1 d（D0），术后1 d（D1），以及术后30 d（D30）的认知评估结果。计算所有患者D0时MoCA评分的标准差。如果术后30 d MoCA评分有1个或多个标准差下降，则诊断为POCD[7]。比较术前、术后认知功能的变化，评价2组POCD的发生情况。

1.4　统计学分析

采用SPSS 25.0软件进行统计分析。分类变量比较采用χ^2或Fisher精确概率法。数值变量采用Kolmogorov-Smirnov检验进行正态分布检验。正态分布

变量以$\bar{x} \pm s$表示，并采用t检验进行比较。非正态分布变量以$M(P_{25}\sim P_{75})$表示，并采用Man-Whitney U检验或Wilcoxon检验进行比较。$P<0.05$为差异有统计学意义。

2　结果

2.1　2组患者一般情况比较

2组患者的年龄、性别、体质量指数、ASA分级、合并疾病、吸烟史、手术和麻醉时间、血红蛋白含量、输液量和失血量比较，差异均无统计学意义（$P>0.05$），具有可比性。见表1。

2.2　2组血流动力学指标比较

D组在T2时点MAP明显高于C组，差异有统计学意义（$P<0.05$），在T3、T4时点MAP明显低于C组，差异有统计学意义（$P<0.05$）。D组在T1、T3、T4时点HR明显低于C组，差异有统计学意义（$P<0.05$）。D组SD_{MAP}和SD_{HR}均明显低于C组，差异有统计学意义（$P<0.05$）。见表2、3。

2.3　2组患者麻醉药和血管活性药的使用量比较

D组丙泊酚和瑞芬太尼总用量均显著低于C组，差异有统计学意义（$P<0.05$）。C组患者去甲肾上腺素和乌拉地尔的使用量均明显高于D组，差异有统计学意义（$P<0.05$）。见表4。2组阿托品和艾司洛尔的使用量比较，差异无统计学意义（$P>0.05$）。

表1　2组患者一般资料和术中观察指标比较

Tab.1　Comparison of patient characteristics and intraoperative indices

Item	Group D (n = 52)	Group C (n = 54)	$t/\chi^2/Z$	P
Age (year)	69.5 (67–73)	69 (67–72)	–0.663	0.507
Sex [n (%)]				
Male	32 (61.5)	39 (72.2)	1.367	0.242
Female	20 (38.5)	15 (27.8)		
BMI (kg/m^2)	23 (21–25)	23 (21–25)	–0.509	0.611
ASA grading [n (%)]				
Ⅱ	35 (67.3)	39 (72.2)	0.304	0.582
Ⅲ	17 (32.7)	15 (27.8)		
HT history [n (%)]	36 (69.2)	31 (57.4)	1.592	0.207
DM history [n (%)]	12 (23.1)	12 (22.2)	0.011	0.916
HLP history [n %)]	14 (26.9)	19 (35.2)	0.843	0.358
Smoking history [n (%)]	17 (32.7)	18 (33.3)	0.005	0.944
Surgical duration (min)	72.56 ± 11.07	74.98 ± 11.85	–1.087	0.279
Anesthetic duration (min)	100.82 ± 16.12	104.70 ± 16.01	–1.246	0.216
Hb (g/L)	131.37 ± 10.53	131.76 ± 12.10	–0.178	0.859
Fluid infusion volume (mL)	840.38 ± 148.54	879.63 ± 205.24	–1.124	0.264
Blood loss (mL)	50 (20–70)	60 (40–80)	–1.549	0.121

BMI, body mass index; ASA, American Society of Anesthesiologists; HT, hypertension; DM, diabetes mellitus; HLP, hyperlipidemia; Hb, hemoglobin; PACU, postanesthesia care unit.

表2　2组MAP和HR比较（$\bar{x} \pm s$）

Tab.2　Comparison of MAP and HR between groups ($\bar{x} \pm s$)

Item	MAP (mmHg)				HR (beats/min)			
	Group D	Group C	t	P	Group D	Group C	t	P
T0	85.69 ± 13.39	82.87 ± 12.17	1.136	0.258	65.52 ± 5.84	65.72 ± 5.71	–0.181	0.857
T1	70.31 ± 5.63	67.80 ± 8.13	1.842	0.068	72.12 ± 5.55	77.76 ± 6.45	–4.819	<0.001
T2	64.92 ± 5.44	57.15 ± 4.66	7.915	<0.001	65.69 ± 5.83	67.52 ± 9.22	–1.213	0.228
T3	72.56 ± 4.14	76.80 ± 7.32	–3.650	<0.001	63.60 ± 7.36	68.78 ± 8.24	–3.410	0.001
T4	77.71 ± 6.80	84.28 ± 11.15	–3.644	<0.001	69.02 ± 6.13	76.41 ± 7.36	–5.605	<0.001

表3　2组SD_{MAP}和SD_{HR}比较

Tab.3　Comparison of SD_{MAP} and SD_{HR} between the two groups

Item	Group D	Group C	*t*/*Z*	*P*
SD_{MAP}	8.48 ± 3.83	11.44 ± 4.32	−3.725	<0.001
SD_{HR}	4.16 (2.30–4.83)	6.03 (5.16–4.27)	−6.699	<0.001

2.4　2组各时点rSO_2、SD_{rSO_2}和认知功能比较

与T0相比，D组和C组的rSO_2在T1~T3时点均明显降低，差异有统计学意义（$P < 0.05$）；在T0~T4各时点2组rSO_2比较无统计学差异（$P > 0.05$）；D组SD_{rSO_2}明显低于C组，差异有统计学意义（$P < 0.05$）。2组患者D0时MoCA评分差异无统计学意义（$P > 0.05$）；D组在D1时的MoCA评分明显高于C组，差异有统计学意义（$P < 0.05$）；D组在D30时POCD发生率明显低于C组，差异有统计学意义（$P < 0.05$）。见表5、6。

2.5　2组气管拔管时间和PACU停留时间比较

表4　2组患者麻醉药和血管活性药的使用量比较

Tab.4　Comparison of anesthetics and vasoactive drugs between the two groups

Item	Group D	Group C	*t*/*Z*	*P*
Propofol (mg)	317.08 ± 16.81	396.06 ± 42.33	−12.534	<0.001
Remifentanil (mg)	0.62 ± 0.08	0.79 ± 0.15	−7.491	<0.001
Norepinephrine (μg)	69.92 ± 11.27	79.56 ± 21.52	−2.871	0.005
Urapidil (mg)	15 (10–20)	25 (15–30)	−3.668	<0.001

表5　2组患者rSO_2比较（$\bar{x} \pm s$）

Tab.5　Comparison of rSO_2 between the two groups（$\bar{x} \pm s$）

Time point	Group D	Group C	*Z*	*P*
T0	0.72 ± 0.020	0.73 ± 0.013	−1.949	0.051
T1	0.71 ± 0.021	0.70 ± 0.019	−0.538	0.591
T2	0.68 ± 0.018	0.68 ± 0.018	−1.242	0.214
T3	0.71 ± 0.017	0.71 ± 0.016	−1.885	0.059
T4	0.72 ± 0.016	0.72 ± 0.018	−1.925	0.054

表6　2组患者认知功能比较

Tab.6　Comparison of cognitive function between the two groups

Item	Group D	Group C	χ^2/*Z*	*P*
SD_{rSO_2}	0.016 (0.012–0.023)	0.019 (0.016–0.026)	−2.883	0.004
MoCA score on D0	24 (23–25)	25 (23–26)	−1.348	0.178
MoCA score on D1	24 (23–25)	22 (21–24)	−2.530	0.011
Incidence of POCD on D30 [*n* (%)]	2 (3.8)	9 (16.7)	−3.131	0.030

D组气管拔管时间明显短于C组，差异有统计学意义（$P < 0.05$）。2组在PACU的停留时间比较，差异无统计学意义（$P > 0.05$）。见表7。

3　讨论

血流动力学不稳定的现象在行CAS患者中普遍存在。39%的患者在术中发生高血压，18.8%~56.1%

表7　2组患者气管拔管时间和PACU停留时间的比较

Tab.7　Comparison of extubation time and time spent in PACU between the two groups

Item	Group D	Group C	*t*/*Z*	*P*
Extubation time (min)	16.65 ± 5.09	19.78 ± 5.70	−2.974	0.004
PACU time (min)	30 (28–35)	30 (26–30)	−1.584	0.113

的患者发生低血压，并可能导致POCD[8-9]。在CAS中，稳定的血流动力学对维持脑血流灌注，保护大脑免受出血性或缺血性损伤，从而减少POCD的发生至关重要[10-11]。右美托咪定是CAS常用药物[13]，然而，右美托咪定的常规推荐剂量可诱发老年患者尤其是有合并症的患者血流动力学波动[4,6]。

本研究结果显示，与术前基线水平相比，2组的术中血流动力学指标均有波动，但D组的血流动力学波动指标（SD_{MAP}和SD_{HR}）明显低于C组，提示超低剂量右美托咪定输注具有维持血流动力学稳定性的作用。可能的机制包括右美托咪定能够降低交感神经张力和抑制去甲肾上腺素的释放，终止疼痛信号的传导，发挥镇痛作用[6]；右美托咪定激动突触后膜α2受体，在抑制交感神经活性的同时加强了迷走神经心脏反射，对血流动力学改变的影响呈剂量-效果依赖模式，本研究中使用的超低剂量低于推荐使用剂量的低限，在一定程度上减少了血流动力学的波动。

CAS需要行控制性降压，因此要适度加深麻醉或给予血管活性药物。在麻醉深度一致的情况下，D组麻醉药物的使用量明显低于C组，与既往研究[12-13]结论相似。右美托咪定减少麻醉药物剂量的机制与其作用于脊髓α2肾上腺素能受体的镇静、镇痛作用有关[14]。D组血管活性药物的使用量较少，证实了右美托咪定的血流动力学稳定作用。

本研究结果显示，D组SD_{rSO_2}明显低于C组，说明右美托咪定可能具有维持正常血供，保护脑组织血流灌注的作用[15]。在术后第1天，D组MoCA评分优于C组，术后30 d的POCD发生率也显著低于C组，进一步说明右美托咪定可能有利于神经功能的早期恢复。右美托咪定改善认知功能的机制可能在于：(1) 右美托咪定通过抑制炎症介质来改善神经炎症行为，控制凋亡信号通路，减少氧自由基的生成；(2) 促进脑源性神经营养因子（brain-derived neurotrophic factor，BDNF）表达的上调，发挥神经保护作用；(3) 右美托咪定能减少儿茶酚胺的释放，有效保护海马区神经元，显著减少神经损伤后的神经退行性变，减少受损脑组织坏死，缓解缺血/再灌注损伤，改善神经功能，缩短POCD的持续时间[6,16]。

本研究结果显示，D组气管拔管时间较C组明显缩短，且没有增加患者在PACU的停留时间，提示右美托咪定对老年患者具有肺保护作用和安全的镇静作用，能够促进术后早期恢复[17-18]。综上所述，持续输注超低剂量右美托咪定可改善CAS老年患者血流动力学的稳定性，保护脑组织血流灌注，促进术后认知功能恢复。

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