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不同浓度的右美托咪定对老年腰椎术患者的镇静效果、氧化应激和血流动力学的影响*

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摘要 目的：探讨不同浓度的右美托咪定对老年腰椎术患者的镇静效果、氧化应激和血流动力学的影响。**方法：**选取2013年3月-2018年4月期间我院收治的老年腰椎术患者90例为研究对象。根据随机数字表法将患者分为对照组(n=30)、低浓度组(n=30)以及高浓度组(n=30)。低浓度组麻醉诱导前输注0.5 μg/kg右美托咪定，高浓度组输注1 μg/kg右美托咪定，对照组不输注右美托咪定。比较给药前(T0)、给药后10 min(T1)、给药后30 min(T2)、给药后60 min(T3)的听觉诱发电位指数(AAI)、改良/镇静视觉评分(OAA/S)。比较T0、T3、手术后24h(T4)的三组患者丙二醛(MDA)、超氧化物歧化酶(SOD)水平。比较T0-T3时间点三组患者的心率(HR)、平均动脉压(MAP)情况。观察三组患者术后不良反应发生情况。**结果：**与T0时间点比较，三组T1-T3时间点AAI、OAA/S均显著降低(*P<0.05*)；与对照组相比，低浓度组与高浓度组T1-T3时间点AAI、OAA/S均较低，且高浓度组低于低浓度组(*P<0.05*)。与T0时间点比较，三组T3、T4时间点MDA均显著升高，T3时间点SOD显著降低(*P<0.05*)；与对照组相比，低浓度组与高浓度组T3、T4时间点MDA均降低，且高浓度组低于低浓度组(*P<0.05*)；高浓度组T3、T4时间点SOD高于低浓度组和对照组(*P<0.05*)。与T0时间点比较，三组T2、T3时间点HR、MAP均降低(*P<0.05*)；与对照组相比，低浓度组、高浓度组T2、T3时间点HR均降低，且高浓度组低于低浓度组(*P<0.05*)；与对照组相比，低浓度组、高浓度组T2、T3时间点MAP均降低，但高浓度组高于低浓度组(*P<0.05*)。三组患者术后不良反应总发生率比较差异无统计学意义(*P>0.05*)。**结论：**1μg/kg右美托咪定对老年腰椎术患者的镇静效果较好，可有效维持血流动力学稳定，减轻氧化应激反应。

关键词：右美托咪定；老年；腰椎术；镇静效果；氧化应激；血流动力学

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Effects of Different Concentrations of Dexmedetomidine on Sedation, Oxidative Stress and Hemodynamics in Elderly Patients Undergoing Lumbar Surgery*

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ABSTRACT Objective: To investigate the effects of different concentrations of dexmedetomidine on sedation, oxidative stress and hemodynamics in elderly patients undergoing lumbar surgery. **Methods:** 90 cases of elderly lumbar spine surgery in our hospital from March 2013 to April 2018 were selected as research subjects. According to the number table method, the patients were randomly divided into control group (n=30), low concentration group (n=30) and high concentration group (n=30). The control group did not receive dexmedetomidine, the low concentration group was given 0.5 μg/kg dexmedetomidine, and the high concentration group was given 1 μg/kg dexmedetomidine. The auditory evoked potential index (AAI), modified / sedative visual score (OAA/S) before administration (T0), 10 min after administration (T1), 30 min after administration (T2), 60 min after administration (T3), and 60 min after administration (T3) were compared. malondialdehyde (MDA) and superoxide dismutase (SOD) were compared between T0, T3 and 24h after operation (T4). The heart rate (HR) and mean arterial pressure (MAP) of T0-T3 time points were compared. The incidence of postoperative ADR in the two groups were observed. **Results:** Compared with T0 time point, AAI and OAA/S at T1-T3 time points in the three groups were significantly reduced (*P<0.05*), compared with the control group, AAI, OAA/S at T1-T3 time points in low concentration group and high concentration group were lower, while the high concentration group were lower than that in low concentration group(*P<0.05*). Compared with the T0 time point, the three groups of T3 and T4 time points MDA increased significantly, SOD at T3 time point significantly decreased (*P<0.05*). Compared with the control group, the T3 and T4 time point MDA in the low concentration group and the high concentration group decreased, and the high concentration group was lower than that of the low concentration group (*P<0.05*), and SOD of T3 and T4 in the high concentration group was higher than that of the low concentration group and the control group (*P<0.05*). Compared with the time point of T0, the three groups of T2 and T3 time points HR and MAP decreased (*P<0.05*). Compared with the

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control group, HR at the T2 and T3 time points in the low concentration group and the high concentration group decreased, and the high concentration group was lower than the low concentration group (*P<0.05*). Compared with the control group, the T2 and T3 time points of MAP in low concentration group and high concentration group decreased, but the high concentration group were higher than those in low concentration group (*P<0.05*). There was no significant difference in the incidence of adverse reactions between the three groups (*P>0.05*). **Conclusion:** 1 μg/kg dexmedetomidine has better sedative effect in elderly patients undergoing lumbar surgery, which can effectively maintain hemodynamic stability and relieve oxidative stress. Dative stress and do not increase postoperative adverse reactions. It has certain clinical value.

Key words: Dexmedetomidine; Elderly; Lumbar surgery; Sedation effect; Oxidative stress; Hemodynamics

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前言

腰椎间盘突出以及腰椎骨折为老年人群的常见病，通常患者会出现腰痛、下肢疼痛等临床症状，给患者日常生活带来严重影响[1,2]。针对该类疾病多采取手术治疗，然而由于腰椎术创伤大、刺激程度高，具有较高的死亡率，加之老年人群身体机能退化，免疫力降低，且存在多种合并症，手术耐受性较差，因此，老年群体的围术期处理已成为临床的研究热点[3,4]。右美托咪定是 α2 肾上腺素能受体激动剂，具有高效性、高特异性以及高选择性，因其具有镇静、镇痛、抗焦虑等作用，常用于临床麻醉、重症监护中[5,6]。然而目前临床关于腰椎术中右美托咪定的具体用量尚存在一定争议。鉴于此，本研究通过探讨不同浓度的右美托咪定对老年腰椎术患者的镇静效果、氧化应激和血流动力学的影响，以期为临床麻醉剂量选择提供参考，现作如下报道。

1 资料与方法

1.1 一般资料

选取 2013 年 3 月 -2018 年 4 月期间我院收治的老年腰椎术患者 90 例为研究对象。纳入标准：(1)患者年龄≥ 60 岁；(2)符合手术指征者；(3)无精神病史可配合本次研究者；(4)患者及其家属知情本研究并签署同意书。排除标准：(1) 合并高血压、心肺疾病者；(2)伴有糖尿病或糖耐量异常者；(3)合并脑卒中、脑损伤病史者；(4)近期服用过抗炎类药物者；(5)围术期发生不良事件者。根据随机数字表法将患者分为对照组(n=30)、低浓度组(n=30)以及高浓度组(n=30)。其中对照组男 17 例，女 13 例，年龄 60-79 岁，平均(69.03± 3.09)岁；腰椎间盘突出患者 12 例，腰椎骨折患者 9 例，腰椎结合患者 9 例。低浓度组男 16 例，女 14 例，年龄 61-83 岁，平均(70.21± 2.78)岁；腰椎间盘突出患者 11 例，腰椎骨折患者 11 例，腰椎结合患者 8 例。高浓度组男 15 例，女 15 例，年龄 62-78 岁，平均(71.28± 2.90)岁；腰椎间盘突出患者 10 例，腰椎骨折患者 9 例，腰椎结合患者 11 例。三组患者一般资料比较差异无统计学意义(*P>0.05*)，具有可比性，本次研究已通过我院伦理委员会批准同意。

1.2 治疗方法

所有患者术前肌注 0.5 mg 阿托品，入室后均开放静脉通路，常规监测心率(heart rate，HR)、平均动脉压(mean arterial pressure，MAP)、心电图、脉搏血氧饱和度等。低浓度组于麻醉诱导前 10 min 静脉输注盐酸右美托咪定注射液（江苏恩华药业股份有限责任公司，国药准字：H20110085)0.5 μg/kg，高浓度组输注剂量为 1.0 μg/kg，持续输注至术前 20 min，对照组未输注右美托咪定。三组患者采用相同的麻醉诱导方法，具体如下：依次静脉注射枸橼酸舒芬太尼（宜昌人福药业有限责任公司，国药准字：H20050580)5 μg/kg，维库溴铵(山西振东泰盛制药有限公司，国药准字：H20065437)0.15 mg/kg，丙泊酚(西安立邦制药有限公司，国药准字：H20010368)0.5-1 mg/kg。诱导后行气管插管，连接麻醉机，调整呼吸参数，潮气量控制在 8-10 mL/kg，呼吸频率控制在 10-12 次 /min，呼气末二氧化碳分压维持在 35 mmHg 左右，吸呼比为 1：2。麻醉维持采用瑞芬太尼 0.15-0.20 μg/(kg·min)，异丙酚 6-8 mg/(kg·h)，顺式阿曲库铵 0.06-0.08 mg/(kg·h)。术后观察患者麻醉恢复情况，拔管后 1h 内无异常可送回病房。

1.3 观察指标

1.3.1 镇静效果 于给药前(T0)、给药后 10 min(T1)、给药后 30 min(T2)、给药后 60 min(T3)采用 A-Line 麻醉深度监护仪监测听觉诱发电位指数（A-line ARX index，AAI），采用改良 / 镇静视觉评分（observer's assessment of alert/sedation，OAA/S）进行镇静评估。AAI 不同意识状态用 0-100 分表示：正常清醒状态（60-100 分）、嗜睡状态（40-59 分）、浅麻醉状态(30-39 分)、临床麻醉状态（10-29 分）、深麻醉状态（10 分以下）。OAA/S 评分标准如下：清醒、对呼名反应迅速(5 分)、对呼名反应迟钝(4 分)、仅对大声呼名有反应(3 分)、意识消失、对大声呼名没反应(2 分)、轻拍身体无反应(1 分)。

1.3.2 氧化应激 检测 T0、T3、手术后 24h(T4)的丙二醛(malondialdehyde，MDA)、超氧化物歧化酶(superoxide dismutase，SOD）水平，分别于上述时间点采集患者静脉血 4 mL，3000 r/min 离心 10 min，取上清液置于 -70℃冰箱中待测。MDA 水平检测采用硫代硫酸巴比妥法，SOD 水平检测采用黄嘌呤氧化酶法，试剂盒购自深圳晶美生物工程有限公司。

1.3.3 血流动力学 观察并记录 T0-T3 时间点的 HR、MAP 情况。

1.3.4 不良反应 观察两组患者术后不良反应发生情况。

1.4 统计学方法

研究数据录入 SPSS23.0 软件处理。计数资料以率(%)表示，采用卡方检验。计量资料用均数± 标准差($\bar{x}\pm s$)表示，采用 t 检验。检验水准 α=0.05。

2 结果

2.1 三组患者镇静效果比较

与 T0 时间点比较，三组 T1-T3 时间点 AAI、OAA/S 均显

著降低（*P<0.05*）；与对照组相比，低浓度组与高浓度组 T1-T3 时间点 AAI、OAA/S 均较低，且高浓度组低于低浓度组（*P<0.05*）；详见表 1。

表 1 三组患者镇静效果比较（$\bar{x}\pm s$，n=30）

Table 1 Comparison of the sedative effects of the three groups（$\bar{x}\pm s$, n=30）

Time	AAI(score)			OAA/S(score)		
	Control group	Low concentration group	High concentration group	Control group	Low concentration group	High concentration group
T0	88.43± 4.12	91.01± 4.83	89.83± 3.63	5.74± 0.58	5.63± 0.72	5.66± 0.63
T1	85.32± 5.12*	65.89± 3.55*#	60.14± 7.87*#&	5.23± 0.65*	4.74± 0.82*#	4.19± 0.72*#&
T2	69.52± 7.84*	50.08± 6.33*#	44.03± 5.62*#&	4.42± 0.45*	3.26± 0.73*#	2.51± 0.48*#&
T3	66.58± 10.79*	49.74± 4.28*#	43.63± 7.08*#&	2.04± 0.89*	1.07± 0.48*#	0.59± 0.24*#&

Note: compared with T0,*$P<0.05$; compared with control group, #$P<0.05$; compared with low concentration group, &$P<0.05$.

2.2 三组患者氧化应激比较

与 T0 时间点比较，三组 T3、T4 时间点 MDA 均显著升高，T3 时间点 SOD 显著降低（*P<0.05*）；与对照组相比，低浓度组与高浓度组 T3、T4 时间点 MDA 均降低，且高浓度组低于低浓度组（*P<0.05*）；高浓度组 T3、T4 时间点 SOD 高于低浓度组和对照组（*P<0.05*）；详见表 2。

表 2 三组患者氧化应激比较（$\bar{x}\pm s$，n=30）

Table 2 Comparison of the three groups of patients with oxidative stress（$\bar{x}\pm s$, n=30）

Time	MDA（nmol/L）			SOD（U/mL）		
	Control group	Low concentration group	High concentration group	Control group	Low concentration group	High concentration group
T0	5.16± 1.13	5.13± 1.20	5.15± 1.08	44.21± 7.12	45.32± 6.83	45.01± 6.31
T3	9.59± 2.02*	8.37± 1.34*#	7.02± 0.94*#&	31.98± 6.33*	34.53± 7.62*	41.22± 5.45*#&
T4	7.28± 1.55*	6.64± 1.87*#	5.83± 0.65*#&	40.78± 7.25	41.76± 6.25	45.79± 6.32#&

Note: compared with T0,*$P<0.05$; compared with control group,#$P<0.05$; compared with low concentration group, &$P<0.05$.

2.3 三组患者血流动力学比较

与 T0 时间点比较，三组 T2、T3 时间点 HR、MAP 均降低（*P<0.05*）；与对照组相比，低浓度组、高浓度组 T2、T3 时间点 HR 均降低，且高浓度组低于低浓度组（*P<0.05*）；与对照组相比，低浓度组、高浓度组 T2、T3 时间点 MAP 均降低，但高浓度组高于低浓度组（*P<0.05*）；详见表 3。

表 3 三组患者血流动力学比较（$\bar{x}\pm s$，n=30）

Table 3 Comparison of hemodynamic between the three groups（$\bar{x}\pm s$, n=30）

Time	HR（time/min）			MAP（mmHg）		
	Control group	Low concentration group	High concentration group	Control group	Low concentration group	High concentration group
T0	81.98± 7.82	82.34± 9.24	81.29± 8.49	82.18± 4.23	81.04± 3.22	81.31± 4.42
T1	80.82± 7.87	81.53± 9.22	79.16± 9.53	81.78± 4.71	79.43± 5.12	79.36± 4.36
T2	78.02± 6.09*	75.32± 8.92*#	71.48± 8.39*#&	79.49± 4.09*	66.84± 4.19*#	74.26± 5.06*#&
T3	77.64± 6.16*	70.90± 8.12*#	66.31± 7.89*#&	74.59± 3.13*	64.89± 5.18*#	69.52± 3.31*#&

Note: compared with T0,*$P<0.05$; compared with control group, #$P<0.05$; compared with low concentration group, &$P<0.05$.

2.4 三组患者术后不良反应比较

三组患者术后不良反应总发生率比较差异无统计学意义（*P>0.05*）；详见表 4。

3 讨论

腰椎术患者由于手术环境、紧张、害怕手术等因素的刺激，易产生焦虑情绪，全身处于应激状态，导致患者出现血压升高、机体高代谢、心率过快等现象[7,8]。因此，患者手术麻醉前给予一定的药物镇静，可减少应激反应，保证患者安全度过围术期。相较于年轻腰椎术患者，老年腰椎术患者身体机能均有较大的变化，例如心血管方面有血液循环速度减慢、血管不同程度硬化、循环反射迟钝等，在呼吸系统方面患者容易发生肺不张事件、降低化学受体对缺氧反应的敏感度等[9-11]。以上改变均能使老年患者在麻醉过程中延长麻醉药物半衰期、药物在体内的排泄时间，导致老年患者肾功能、肺功能以及循环功能遭受不同程度的损伤，严重影响预后[12-14]。右美托咪定为一种麻醉复合药，主要作用于脑干蓝斑核以及周围神经系统，具有明显镇静、镇痛、抗焦虑功能，同时可通过调控儿茶酚胺的释放从而减轻患

表 4 三组患者术后不良反应比较[n(%)]

Table 4 Comparison of postoperative adverse reactions in the three groups[n(%)]

Groups	Restlessness during the awakening period	Shiver	Vomit	Dry mouth	Hypotension	Bradycardia	Total incidence
Control group(n=30)	3(10.00)	4(13.33)	2(6.67)	3(10.00)	4(13.33)	2(6.67)	18(60.00)
Low concentration group(n=30)	1(3.33)	3(10.00)	2(6.67)	2(6.67)	3(10.00)	3(10.00)	14(46.67)
High concentration group(n=30)	1(3.33)	3(10.00)	1(3.33)	4(13.33)	4(13.33)	2(6.67)	17(56.67)
x^2							1.076
P							0.305

者应激反应[15-17]。

本研究结果表明,与术前比较,三组术后 AAI、OAA/S 均显著降低，且与对照组相比，低浓度组与高浓度组术后 AAI、OAA/S 均较低,且高浓度组低于低浓度组。提示低浓度组与高浓度组均具有一定的镇静、镇痛作用,且高浓度的右美托咪定镇静效果更为明显。葛冬梅等人研究显示右美托咪定存在剂量效应,本研究药效发挥机制与其基本一致[18]。另与术前比较,三组 T3、T4 时间点 MDA 均显著升高,T3 时间点 SOD 显著降低,与对照组相比,低浓度组与高浓度组 MDA、SOD 均有所改善,且高浓度组改善程度优于低浓度组。表明相较于低浓度的右美托咪定,高浓度的右美托咪定减轻老年腰椎术患者氧化应激反应更为显著。氧化应激状态下可产生大量氧自由基,生物分子被氧化受损,进一步导致细胞死亡、组织受损。氧化应激产物中以 MDA 毒性最大,其浓度高低可反映细胞受自由基损伤程度[19,20]。SOD 是细胞内产生的一种天然的氧自由基清除剂,具有机体抵抗和清除自由基等作用,其活性高低可反映机体清除自由基的能力[21]。分析其作用机制,高浓度的右美托咪定进入机体后,与 α2 受体结合,交感神经张力降低,迷走神经活性增强,通过抑制腺苷酸环化酶活性以及环磷腺苷的合成以减少钙离子内流至神经末梢,进而减少递质释放使突触前、后膜超级化,发挥镇静、抗应激反应等作用[22,23]。在血流动力学的比较方面,三组患者术后 HR、MAP 均降低,相较于对照组,低浓度组与高浓度组术后均可以维持 HR、MAP 稳定，且高浓度组维持效果更好。这可能与位于脑干的血管舒缩中枢的 α2AR 结合,并抑制中枢去甲肾上腺素的合成与释放,使交感中枢的张力下降有关[24,25]。同时三组患者术后不良反应总发生率比较差异无统计学意义。表明高浓度右美托咪定安全性较好,不会增加不良反应发生率。

综上所述，老年患者腰椎术中使用高浓度右美托咪定,镇静效果较好,有利于稳定术中血流动力学,减轻患者术后氧化应激反应,且不增加术后不良反应发生率。

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