doi: 10.13241/j.cnki.pmb.2019.01.013

右美托咪定对低血红蛋白全麻患者脑氧饱和度及术后认知功能的影响 *

黄 昕[1] 白文娅[2] 常媛媛[3] 滕秀飞[3] 杨延超[3] 万玉骁[3] 李 阳[3] 朱俊超[3]

(1 华中科技大学同济医学院附属协和医院 湖北 武汉 430022；

2 昆明医科大学第一附属医院 云南 昆明 650000；3 中国医科大学附属盛京医院 辽宁 沈阳 110004)

摘要 目的：探讨右美托咪定对低血红蛋白全麻患者脑氧饱和度及术后认知功能的影响。**方法：**选取择期在全麻行开腹妇科手术、血红蛋白 8～9 g/dl 的患者 30 例，ASA 分级 I～II 级，将其随机分成两组：生理盐水组(N 组)和右美托咪啶组(D 组)，每组 15 例。两组麻醉诱导后，均行七氟醚复合瑞芬太尼静吸复合麻醉维持。D 组在麻醉诱导前经 15 min 静脉输注右美托咪定 0.5 μg/kg，继之以 0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$ 的速率输注至术毕，N 组给予等容量生理盐水。分别于入室时(T_0)、吸氧后 3 min(T_1)、手术开始即刻(T_2)、手术开始后 10 min(T_3)、20 min(T_4)、30 min (T_5)、手术结束即刻(T_6)以及患者苏醒拔管后 5 min(T_7)记录平均动脉压(Mean Arterial Pressure，MAP)、心率(Heart Rate，HR)、血氧饱和度(Percutaneous Oxygen Saturation，SpO_2)、呼吸末二氧化碳分压(End-Tidal Carbon Dioxide Partial Pressure，$PETCO_2$)、脑氧饱和度(Regional Cerebral Saturation Of Oxygenation，rSO_2)、脑电双频指数(Bispectral Index，BIS)以及腋温。并于术前 1 d、术后 1 d 以及术后 3 d，记录蒙特利尔认知评估量表(Montreal Cognitive Assessment，MoCA)数值以及术后认知功能障碍(Postoperative Cognitive Dysfunction,POCD)的发生率。**结果：**与 N 组比较，D 组在 T_2~T_6 时的 rSO_2 升高，HR 降低($P<0.05$)，两组各时点 MAP、SpO_2、$PETCO_2$、BIS 以及腋温比较差异无统计学意义 ($P>0.05$)。与 N 组比较，D 组术后 1 天、术后 3 天 MoCA 评分均显著升高，且术后认知功能障碍的发生率明显降低($P<0.05$)。**结论：**右美托咪定能够提高低血红蛋白患者的脑氧饱和度，改善患者脑氧供需平衡，降低术后认知功能障碍的发生率。

关键词：脑氧饱和度；右美托咪定；血红蛋白；术后认知功能障碍

中图分类号：R614.2；R713 **文献标识码：**A **文章编号：**1673-6273(2019)01-63-05

Effects of Dexmedetomidine on the Cerebral Oxygen Saturation and Postoperative Cognitive Function of Patients with Low Hemoglobin*

HUANG Xin[1], BAI Wen-ya[2], CHANG Yuan-yuan[3], TENG Xiu-fei[3], YANG Yan-chao[3], WAN Yu-xiao[3], LI Yang[3], ZHU Jun-chao[3]

(1 Union Hospital Affiliated to Tongji Medical college of Huazhong University of Science and Technology, Wuhan, Hubei, 430022, China;

2 First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan, 650000, China;

3 Shengjing Hospital of China Medical University, Shenyang, Liaoning, 110004, China)

ABSTRACT Objective: To investigate the effects of dexmedetomidine on cerebral oxygen saturation and postoperative cognitive function ofpatients with low hemoglobin. **Methods:** Thirty female patients, with hemoglobin concentration of 8-9 g/dl, aged 50-65 yr, weighing 50 - 80 kg, of American Society of Anesthesiologists physical status I or II, scheduled for elective gynecologic operation were randomly divided into 2 groups (n = 15 each) using a random number table: normal saline group (group N) and dexmedetomidine group (group D). After anesthesia induction the two groups all underwent sevoflurane and remifentanil intravenous-inhalation combined anesthesia, patients in group D were given dexmedetomidine infused intravenously at a dose of 0.5 μg/kg over 15 min, before induction of anesthesia, followed by 0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$ infusion until the end of surgery, patients in group N were given an equivalent amount of normal saline infusion. Before induction of anesthesia(baseline, T_0), at 3 min after the oxygen inhalation(T_1), at immediately and 10 min, 20 min, 30 min after the start of the operation ($T_{2\text{-}5}$), at the end of the operation (T_6), and at 5 min after extubation (T_7), the mean arterial pressure (MAP), heart rate (HR), percutaneous oxygen saturation (SPO_2), end-tidal carbon dioxide partial pressure ($PETCO_2$), cerebral oxygen saturation(rSO_2), bispectral index(BIS), body temperature were recorded. At 1 day before the start of the operation, at 1 day, 3 day after the operation the score of Montreal Cognitive Assessment (MoCA), and the incidence of postoperative cognitive dysfunction (POCD) were also recorded. **Results:** Compared with group N, the rSO_2 was significantly increased, the HR was decreased at the time point of T_2~T_6 in group D ($P<0.05$). There was no significant difference in the comparison of MAP, SpO_2, $PETCO_2$, BIS and axillary temperature between the two groups ($P>0.05$). Compared with group N, the score of MoCA at 1day, 3day after the operation was higher, and the incidence of POCD was lower in group D($P<0.05$). **Conclusions:** Dexmedetomidine can improve the cerebral oxygen saturation in patients with low hemoglobin, as well as improving the cerebral oxygen balance, and reduce the incidence rate of POCD of patients

* 基金项目：辽宁省自然科学基金项目(20102282)

作者简介：黄昕(1991-)，女，七年制硕士，住院医师，E-mail: 1026688964@qq.com

△通讯作者：朱俊超(1974-)，女，博士，教授，麻醉科副主任，E-mail: zhujunchao1@hotmail.com

(收稿日期：2018-03-08 接受日期：2018-03-31)

with low hemoglobin.

Key words: Cerebral oxygen saturation; Dexmedetomidine; Hemoglobin concentration; Postoperative cognitive dysfunction

Chinese Library Classification(CLC): R614.2; R713 **Document code:** A

Article ID: 1673-6273(2019)01-63-05

前言

脑氧饱和度通过近红外光谱技术测得[1,2],可及时反映术中脑组织的氧供需平衡动态变化,对改善患者术后认知功能障碍及预后起重要作用[3,4]。血红蛋白是脑氧饱和度的一个重要影响因素。K. Yoshitani 等[5]学者发现血红蛋白与患者脑氧饱和度呈正相关。右美托咪定,可以通过激动 α2- 肾上腺素能受体,来发挥改善颅脑功能、降低脑氧代谢率、有助于维持脑氧供需平衡以及改善术后认知功能等作用[6]。有研究表明术中应用右美托咪定能够提高患者围术期颈静脉球氧饱和度[7-10]。颈静脉球氧饱和度和脑氧饱和度有很强的相关性,均可以反映脑氧供需平衡状态[11]。然而,有关右美托咪定在血红蛋白减低患者中应用能否提高脑氧饱和度、改善脑氧供需平衡,进而起到脑保护作用目前尚无定论。本研究旨在探讨右美托咪定对低血红蛋白全麻患者脑氧饱和度及术后认知功能的影响,为临床提供参考。

1 资料与方法

1.1 病例纳入与排除标准

本研究已获中国医科大学附属盛京医院医学伦理委员会批准并与患者签署知情同意书。选取在我院择期行全麻开腹妇科手术, 血红蛋白在 8~9 g/dl 的患者 30 例,ASA 分级 I~II 级、年龄 50~65 岁、身高 155~170 cm、体重 50~80 kg。采用计算机随机数字表法随机分为两组:生理盐水组(N 组)和右美托咪啶组(D 组),每组 15 例。排除标准:术前服用过神经精神类药物;存在系统性呼吸系统、循环系统或中枢神经系统疾病患者;术前 MOCA 评分小于 26 分、基线脉搏血氧饱和度<98%、对 BIS 监测以及脑氧饱和度监测存在低反应性、或前额区面积<6.5 cm^2;血流动力学不稳定患者,即术中出现平均动脉压与基线比较大于± 25%,并持续超过 3 min;术毕测患者血红蛋白与术前比较相差大于± 0.5 g/dl。

1.2 麻醉方法

所有患者进入手术室前均不给予术前用药,并且禁食 8 h、禁饮 4 h。两组患者入室后常规连接心电图、血压、脉搏血氧饱和度,连接 BIS 监测仪器以及脑氧饱和度检测仪,脑氧饱和度探头放置在右前额,BIS 监测探头放置在脑氧饱和度监测仪的下方、眉缘上方。在探头放置部位用酒精擦拭皮肤,待干后放置。分别建立患者动静脉通路,采血气测患血红蛋白。记录患者的基本信息,包括患者性别、年龄、体重、身高、头围、术前血红蛋白。进行充分预充氧后,D 组在麻醉诱导前给予右美托咪定(浓度:4 μg/mL, 负荷剂量:0.5 μg/kg, 并于 15 min 内静脉泵入)。N 组给予等容量的 0.9%生理盐水。两组患者均给予舒芬太尼 0.2 μg/kg、依托咪酯 0.2 mg/kg 行麻醉诱导。待睫毛反射消失后静推顺式阿曲库铵 0.2 mg/kg。约两分钟后待肌松完全及循环稳定后插入喉罩,并固定。给予机械通气:参数为:潮气量 7 mL/kg、呼吸频率 12 次 /min、吸呼比 1:2、呼吸末正压通气调到零、氧 / 空气混合(1:1)。术中根据情况调整潮气量和呼吸频率维持呼吸末二氧化碳分压 (pressure of end-tidal carbon dioxide, $PETCO_2$)在 35 ~ 40 mmHg。两组均采用七氟醚复合瑞芬太尼进行麻醉维持,根据 BIS 调整麻醉药物的浓度,维持 BIS 值在 45~55 之间, D 组术中持续泵入配成 4 μg/ml 浓度右美托咪定,以 0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$ 速度泵入至术毕。N 组持续泵入等量的生理盐水。根据手术情况间断追加顺式阿曲库铵,维持血流动力学稳定,保持 MAP 波动在基础值的 25%以内,维持术中 SpO_2 98%。如果给药期间血压低于基础值 25%,给予麻黄素 5 mg 静注;当心率低于 50 次 / 分,给予阿托品 0.3 mg 静注。术毕前 30 min,给予舒芬太尼 5 μg,使术后 VAS 评分 3 分。于手术结束即刻采血气,测患者血红蛋白浓度。

1.3 检测指标

分别于入室时(T_0)、吸氧后 3 min(T_1)、手术开始即刻(T_2)、手术开始后 10 min(T_3)、20 min (T_4)、30 min(T_5)、手术结束即刻(T_6)以及患者苏醒拔管后 5 min(T_7)记录 MAP、HR、SpO_2、$PETCO_2$、rSO_2、BIS 以及腋温。并于术前 1 d、术后 1 d 以及术后 3 d 记录 MoCA 数值。MoCA 评分低于 26 分或低于术前基础值 2 分记为该患者发生 POCD,计算出患者手术后 POCD 的发生率。

1.4 统计学分析

采用 SPSS19.0 统计学软件进行分析, 计量资料以均数±标准差($\bar{x}\pm s$)表示,多组间比较采用单因素方差分析,进一步两组间比较采用 SNK-q 检验,以 *P<0.05* 为差异有统计学意义。

2 结果

2.1 两组患者一般资料比较

两组患者一般资料比较差异均无统计学意义(*P > 0.05*),见表 1。

2.2 两组不同时点 MAP、HR、SpO_2、$PETCO_2$、rSO_2、BIS 以及腋温的比较

与 N 组比较,D 组在 T_2~T_6 时的 rSO_2 升高,HR 降低 (*P<0.05*),两组各时点 MAP、SpO_2、$PETCO_2$、BIS 以及腋温比较差异无统计学意义(*P>0.05*),见表 2。

2.3 两组术后 POCD 的发生情况比较

与 N 组比较,D 组术后 1 天、术后 3 天 MoCA 评分均显著升高,且术后认知功能障碍的发生率明显降低(*P<0.05*),见表 3。

3 讨论

有研究表明脑氧饱和度的绝对值小于 50%或低于自身基础值的 20%很容易发生 POCD、中风、肾呼吸衰竭甚至死亡[12],但维持脑氧饱和度在基础值的 10% ~ 20%能够减少并发症[13-15]。由于术中常规监测指标如血压、心电图、脉搏血氧饱和度、呼吸末二氧化碳分压等都不能直观反映患者脑氧输送是否充分,因此术中监测脑氧饱和度现已广泛应用于临床[16]。

表 1 两组患者一般资料比较

Table 1 Comparison of the general information between two groups(n=15, $\bar{x}\pm s$)

Groups	Age (yr)	Weight (kg)	Height (cm)	Head Size (cm)
Group N	57.5± 7.7	62.2 ± 10.3	161.1 ± 4.2	56.5 ± 1.3
Group D	54.1± 8.4	61.5 ± 11.6	163.5 ± 4.5	56.7 ± 0.9

表 2 两组患者在不同时间点观察指标的比较

Table 2 Comparison of the observation index at different timepoints between two groups (n = 15, $\bar{x}\pm s$)

Index	Groups	T_0	T_1	T_2	T_3	T_4	T_5	T_6	T_7
MAP (mmHg)	Group N	104.1± 15.2	97.3± 13.1	84.8± 10.3	88.3± 11.5	84.3± 6.6	90.8± 7.7	86.4± 7.6	97.8± 6.3
	Group D	98.3± 13.5	104.3± 12.2	79.3± 8.5	83.3± 10.0	81.4± 9.2	85.3± 10.2	82.3± 11.1	93.3± 5.2
HR (beats/min)	Group N	75.1± 12.3	78.5± 12.1	74.1± 8.2	72.3± 9.7	75.2± 8.3	70.3± 9.8	74.3± 8.1	77.7± 11.1
	Group D	80.3± 13.4	76.3± 10.6	66.2± 9.1[a]	62.2± 7.7[a]	70.1± 6.3[a]	63.1± 8.0[a]	66.0± 9.1[a]	81.4± 11.3
SpO_2 (%)	Group N	99.2± 0.6	99.4± 0.4	99.3± 0.4	99.4± 0.4	99.4± 0.4	99.4± 0.3	99.4± 0.4	99.4± 0.4
	Group D	99.4± 0.4	99.3± 0.4	99.4± 0.5	99.4± 0.3	99.4± 0.3	99.4± 0.4	99.3± 0.3	99.2± 0.5
rSO_2 (%)	Group N	65.1± 4.0	68.5± 4.3	54.4± 3.7	53.1± 4.2	56.3± 3.6	55.1± 3.3	56.4± 3.1	64.4± 5.6
	Group D	67.5± 5.5	70.1± 4.3	61.1± 3.2[a]	60.0± 3.1[a]	61.8± 4.8[a]	59.5± 4.4[a]	59.7± 3.5[a]	67.7± 5.6
BIS	Group N	91.1± 3.3	93.5± 4.6	50.8± 3.8	50.9± 4.1	48.5± 4.7	50.1± 4.7	52.1± 4.4	90.4± 5.1
	Group D	93.4± 4.6	91.1± 3.8	52.1± 4.7	52.2± 3.3	50.1± 3.5	48.8± 5.3	50.0± 4.1	92.2± 3.3
$P_{Et}CO_2$ (mmHg)	Group N	39.3± 4.1	40.1± 3.4	39.4± 2.3	41.2± 3.1	38.8± 3.1	39.8± 3.1	40.0± 3.5	40.6± 4.5
	Group D	41.2± 4.3	40.2± 4.1	38.9± 3.1	39.8± 4.2	38.4± 4.5	40.2± 3.1	39.1± 3.0	41.2± 5.4
axillary temperature (℃)	Group N	36.2± 0.4	36.4± 0.4	36.2± 0.5	36.3± 0.5	36.1± 0.4	36.3± 0.4	36.4± 0.3	36.1± 0.4
	Group D	36.3± 0.4	36.3± 0.3	36.4± 0.5	36.2± 0.4	36.2± 0.4	36.3± 0.3	36.2± 0.4	36.3± 0.5

Note: Compared with Group N, [a]$P < 0.05$.

表 3 两组患者术后 MoCA 评分和 POCD 发生情况的比较

Table 3 Comparison of the MoCA Score and incidence of POCD after operation between two groups(n = 15)

Groups	At 1 d before the operation	At 1 d after the operation	At 3 d after the operation	The incidence of POCD(%)
Group N	27.7± 1.2	25.7± 1.7	26.5± 1.0	6(40.0%)
Group D	28.1± 1.1	27.1± 1.0[a]	27.7± 1.2[a]	1(6.7%)[a]

Note: Compared with Group N, [a]$P < 0.05$.

血红蛋白是影响脑氧饱和度一个重要因素。目前已有研究表明血红蛋白的降低与脑氧饱和度降低成线性关系[5]。在输血、代偿性或失代偿性失血以及血液稀释等情况下，脑氧饱和度数值与血红蛋白也具有相关性[17-20]。血红蛋白降低可能破坏了脑氧供需平衡，从而导致脑氧饱和度下降。右美托咪定为高选择性 α2 肾上腺能受体激动剂，可抑制手术刺激引起的交感神经系统兴奋、减少儿茶酚胺的合成和释放、稳定围术期的血流动力学、降低脑代谢、维持脑氧的供需趋近平衡[21]。α2 肾上腺素能受体分为 α2A，α2B，α2C 三种亚型。右美托咪定与中枢神经系统蓝斑核内的 α2A 受体结合后可产生剂量依赖的镇静、催眠作用，其中 α2B 受体具有收缩血管、抗寒战和利尿作用，而右美托咪定激活蓝斑核的 α2C 受体，则可以产生抗焦虑作用[22]。

本研究结果显示右美托咪啶组患者在 $T_2 \sim T_6$ 时的脑氧饱和度均显著高于生理盐水组，且 POCD 发生率降低。这可能与右美托咪定具有降低脑血流以及降低脑代谢作用相关。Oak Z 等[23]在小鼠实验模型中研究发现在血红蛋白正常组，右美托咪定能够使区域性脑血流和脑氧耗成比例的下降，而并不影响脑氧饱和度的数值；而在血红蛋白浓度降低组，仅应用盐水的情况下，小鼠的脑血流下降的程度超过脑氧耗，而应用右美托咪定组能够防止脑血流进一步下降。因此，当血红蛋白浓度降低

时,右美托咪定能起到最佳的氧供给,保证氧耗平衡[24]。有文献报道应用较高初始负荷剂量右美托咪定时(1～4 μg/kg),右美托咪定与血管平滑肌的 α2B 受体及突触后膜 α1 受体结合使血管收缩导致血压升高、反射性心率减慢[25]。因此,本实验中设定右美托咪定负荷量的输注时间为 15 min,避免输注时间过快导致血压升高对本实验产生干扰,并且选择右美托咪定负荷量 0.5 μg/kg,维持期间持续输注 0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$ 至术毕,避免过大负荷剂量应用引起血压升高及反射性心率减慢[26]、维持血流动力学稳定。

脑氧饱和度受诸多因素影响,如患者年龄、脑氧饱和度监测仪探头放置的位置[27]、血红蛋白、动脉血氧饱和度、呼吸末二氧化碳分压[28]、吸氧浓度、体温以及脉搏血氧饱和度等都会影响脑氧饱和度的监测结果[29]。因此,在本研究中,我们控制各组之间 BIS 和脑氧饱和度监测仪探头放置位置相对固定,以及控制腋温、脉搏血氧饱和度、呼吸末二氧化碳分压、吸入麻醉药呼吸末浓度以及年龄均在要求范围内并且组间没有统计学差异,以保证研究结果的准确性。此外,本研究发结果显示当患者吸入纯氧后,虽然在入室以及吸氧后 3 min 时的脑氧饱和度差异没有统计学意义,其脑氧饱和度的平均值的确稍高于患者在吸入空气状态下的脑氧饱和度。因此,术中我们控制两组均吸入氧 / 空气混合(1:1)气体以排除吸入氧浓度不同而产生的干扰。

综上所述,右美托咪定可以提高低血红蛋白患者的脑氧饱和度,改善脑氧供需平衡,降低术后认知功能障碍的发生率。

参 考 文 献(References)

[1] Terri M, James M. Understanding near-Infrared Spectroscopy [J]. Advances in Neonatal Care, 2011, 6(11): 382-388

[2] Moerman A, Meert F, De Hert S.Cerebral near-infrared spectroscopy in the care of patients during cardiological procedures: a summary of the clinicalevidence[J]. J Clin Monit Comput, 2016, 30(6): 901-909

[3] Ni C, Xu T, Li N, et a1. Cerebral oxygen saturation after multiple perioperative influential factors predicts the occurrence of postoperativecognitive dysfunction [J]. BMC Anesthesiol, 2015, 15: 156

[4] Zheng F, Sheinberg R, Yee M, et a1. Cerebral near-infrared spectroscopy monitoring and neurologic outcomes in adult cardiac surgery patients. A systematic review [J]. Anesth Analg, 2013, 116 (3): 663-676

[5] K. Yoshitani, M. Kawaguchi, M. Iwata. Comparison of changes in jugular venous bulb oxygen saturation and cerebral oxygen saturation during variations of hemoglobin concentration under propofol and sevoflurane anaesthesia [J]. British Journal of Anaesthesia, 2005, 94 (3): 341-346

[6] 占丽芳,李国强,单热爱,等. 右美托咪定对脑幕上肿瘤切除术患者脑氧代谢的影响[J]. 广东医学, 2014, 35(22): 3481-3484
Zhan Li-fang, Li Guo-qiang, Shan Re-ai, et al. Effects of dexmedetomidine on cerebral oxygen metabolism during supratentorial tumor resection[J]. Guangdong Medical Journal, 2014, 35(22): 3481-3484

[7] JianLu, Gang Chen, Hongmei Zhou, et al. Effect of parecoxib sodium pretreatment combined with dexmedetomidine on early postoperative cognitive dysfunction in elderly patients after shoulder arthroscopy: A randomized double blinded controlled trial [J]. J Clin Anesth, 2017, 41: 30-34

[8] 张光辉, 马文泽, 王虹, 等. 右美托咪定对颅内动脉瘤栓塞术患者围术期脑氧代谢的影响[J]. 中国卫生产业, 2013, 19: 102 - 104
Zhang Guang-hui, Ma Wen-ze, Wang Hong, et al. Effects of dexmedetomidine on cerebral oxygen metabolism during operation period in patients undergoing embolization of intracranial aneurysm [J]. China Health Industry, 2013, 19: 102-104

[9] 邓晰明, 邹琪, 段立彬, 等. 右美托咪定对重型颅脑外伤术后脑氧代谢的影响[J]. 中山大学学报(医学科学版), 2016, 37(4): 630-636
Deng Xi-ming, Zou Qo, Duan Li-bin, et al. Effects on cerebral oxygen metabolism of severe traumatic brain injury after operation treated with dexmedetomidine [J]. Journal of Sun Yat-Sen University (Medical Sciences), 2016, 37(4): 630-636

[10] 韦秋凤, 陈小健, 冯丝丝,等. 右美托咪定对全髋关节置换术患者脑氧代谢与能量代谢的影响 [J]. 广西医科大学学报, 2017, 34(5): 743-745
Wei Qiu-feng, Chen Xiao-jian, Feng Si-si, et al. Effect of dexmedetomidine on cerebral oxygen metabolism and energy metabolism in patients underwent total hip replacement[J]. Journal of Guangxi Medical University, 2017, 34(5): 743-745

[11] Abdul-Khaliq H, Troitzsch D, Berger F, et al. Regional transcranial oximetry with near infrared spectroscopy (NIRS) in comparison with measuring oxygen saturation in the jugular bulb in infants and children for monitoring cerebral oxygenation [J]. BiomedTech(Berl), 2000, 45(11): 328-332

[12] 刘珊珊,李恩有.脑氧饱和度监测在老年患者中的应用进展[J].中华临床医师杂志(电子版), 2013, 7(24): 11798-11800
Liu Shan-shan, Li En-you. The application of monitoring cerebral oxygen saturation in elderly patients [J]. Chin J Clin (Electronic Edition), 2013, 7(24): 11798-11800

[13] Heena Bidd, Audrey Tan, David Green. Using bispectral index and cerebral oximetry to guide hemodynamic therapy in high-risk surgical patients[J]. Perioperative Medicine, 2013, 2(1): 11

[14] Henrik Sørensen, Hilary P. Grocott, Niels H. Secher. Near infrared spectroscopy for frontal lobe oxygenation during non-vascular abdominal surgery[J]. Clin Physiol Funct Imaging, 2016, 36: 427-435

[15] Panzera P, Greco L, Carravetta G, et al. Alteration of brain oxygenation during "piggy back" liver transplantation [J]. Adv Exp Med Biol, 2006, 578: 269-275

[16] Moerman A, De Hert S. Cerebral oximetry: the standard monitor of the future? [J]. Curr Opin Anaesthesiol, 2015, 28(6): 703-709

[17] Torella F, Cowley R, Thorniley MS, et al. Monitoring blood loss with near infrared spectroscopy [J]. Comp Biochem Physiol A Mol Integr Physiol, 2002, 132: 199-203

[18] Torella F, Cowley RD, Thorniley MS, et al. Regional tissue oxygenation during hemorrhage: can near infrared spectroscopy be used to monitor blood loss[J]. Shock, 2002, 18(5): 440-444

[19] Lassnigg A, Hiesmayr M, Keznickl P, et al. Cerebral oxygenation during cardiopulmonary bypass measured by near-infrared spectroscopy: effects of hemodilution, temperature, and flow [J]. J Cardiothorac Vasc Anesth, 1999, 13(5): 544-548

[20] Liem KD, Hopman JC, Oeseburg B, et al. The effect of blood transfusion and haemodilution on cerebral oxygenation and

haemodynamics in newborn infants investigated by near infrared spectrophotometry[J]. Eur J Pediatr, 1997, 156(4): 305-310

[21] 吕安庆，陈文迪. 右美托咪定联合全麻下老年患者术后认知功能与脑氧代谢的关系[J].河北医科大学学报, 2012, 33(3): 299-303
Lv An-qing, Chen Wen-di. Relations the cerebral oxygen metabolism and the cognitive function after combined dexmedetomidine anesthesia operation in elderly patients [J]. Journal of Hebei medical university, 2012, 33(3): 299-303

[22] Maria Wujtewicz1, Dariusz Maciejewski, Hanna Misiołek. Use of dexmedetomidine in the adult intensive care unit[J]. Anaesthesiology Intensive Therapy, 2013, 45(4): 235-240

[23] Oak Z. Chi, Christine Hunter, Xia Liu. et al. The Effects of Dexmedetomidine on Regional Cerebral Blood Flow and Oxygen Consumption During Severe Hemorrhagic Hypotension in Rats [J]. Anesth Analg, 2011, 113(2): 349-355

[24] 王淮, 边卫, 寇党培, 等. 右美托咪啶对体外循环心内直视手术患者脑氧代谢和糖代谢的影响 [J]. 中华麻醉学杂志, 2011, 31(11): 1293-1297
Wang Huai, Bian Wei, Kou Dang-pei, et al. Effects of dexmedetomidine On cerebral oxygen and glucose metabolism in patients undergoing mitral valve replacement under cardiopulmonary bypass[J]. Chin J Anesthesiol, 2011, 31(11): 1293-1297

[25] Ebert TJ, Hall JE, Barney JA. The Effects of Increasing Plasma Concentrations of Dexmedetomidine in Humans [J]. Anesthesiology, 2000, 93(2): 382-394

[26] 杨延超, 朱俊超. 不同剂量右美托咪定对全麻患者镇静效果和血流动力学的影响[J].中国冶金工业医学杂志, 2013, 30(2): 202-205
Yang Yan-chao, Zhu Jun-chao. Effects of different doses of dexmedetomidine on the sedative efficacy and haemodynamics during general anesthesia [J]. Chinese Medical Journal of Metallurgical Industry, 2013, 30(2): 202-205

[27] Kishi K, Kawaguchi M, Yoshitani K et al. Influence of patient variables and sensor location on regional cerebral oxygen saturation measured by INVOS 4100 near-infrared spectrophotometers [J]. J Neurosurg Anesthesiol, 2003, 15(4): 302-306

[28] 贾宝森, 张宏. 脑氧饱和度监测在临床的应用进展[J].武警医学, 2004, 15(10): 781-783
Jia Bao-sen, Zhang Hong. The progress about Monitoring of cerebral oxygen saturation in clinical application [J]. Medical Journal of the Chinese People's Armed Police Forces, 2004, 15(10): 781-783

[29] Jun IG, Shin WJ, Park YS, et al. Factors affecting intraoperative changes in regional cerebral oxygen saturation in patients undergoing liver transplantation[J]. Transplant Proc, 2013, 45(1): 245-250

（上接第 86 页）

[18] Venditti A, Buccisano F, Del Poeta G, et al. Level of minimal residual disease after consolidation therapy predicts outcome in acute myeloid leukemia[J]. Blood, 2000, 96(12): 3948-3952

[19] Kern W, Voskova D, Schoch C, et al. Determination of relapse risk based on assessment of minimal residual disease during completeremission by multiparameter flow cytometry in unselected patients with acute myeloid leukemia [J]. Blood, 2004, 104 (10): 3078-3085

[20] Kern W, Haferlach T, Schoch C, et al. Early blast clearance by remission induction therapy is a major independent prognostic factor for both achievement of complete remission and long-term outcome in acute myeloid leukemia: data from the German AML Cooperative Group (AMLCG) 1992 Trial[J]. Blood, 2003, 101(1): 64-70

[21] Gianfaldoni G, Mannelli F, Bencini S, et al. Peripheral blood blast clearance during induction therapy in acute myeloid leukemia [J]. Blood, 2008, 111(3): 1746-1747

[22] Elliott MA, Litzow MR, Letendre LL, et al. Early peripheral blood blast clearance during induction chemotherapy for acute myeloid leukemia predicts superior relapse-free survival [J]. Blood, 2007, 110 (13): 4172-4174

[23] Maurillo L, Buccisano F, Piciocchi A, et al. Minimal residual disease as biomarker for optimal biologic dosing of ARA-C in patients with acute myeloid leukemia[J]. Am J Hematol, 2015, 90(2): 125-131

[24] Köhnke T, Sauter D, Ringel K, et al. Early assessment of minimal residual disease in AML by flow cytometry during aplasia identifies patients at increased risk of relapse [J]. Leukemia, 2015, 29 (2): 377-386

[25] Walter RB. Should acute myeloid leukemia patients with actionable targets be offered investigational treatment after failing one cycle of standard induction therapy? [J]. Curr Opin Hematol, 2016, 23 (2): 102-107

[26] Geoffrey L. Uy, Eric J. Duncavage, Gue Su Chang, et al. Dynamic Changes in the Clonal Structure of MDS and AML in Response to Epigenetic Therapy [J]. Leukemia, 2017, 31(4): 872-881

[27] Hartmut Döhner, Elihu Estey, David Grimwade, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel[J]. Blood, 2017, 129(4): 424-447