

doi: 10.13241/j.cnki.pmb.2018.03.016

0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ 维持剂量右美托咪定麻醉对肺癌根治术患者血清 IL-6、NSE、S100 β 蛋白水平的影响*

凌 华¹ 刘 斌^{1△} 梁 霄¹ 谢先丰² 谢科宇² 孙 燕²

(1 四川大学华西医院 麻醉科 四川 成都 610041; 2 成都市第二人民医院 麻醉科 四川 成都 610017)

摘要 目的:探讨肺癌根治术应用 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ 维持剂量右美托咪定(Dex)辅助麻醉对患者血清白细胞介素-6(IL-6)、神经元特异性烯醇化酶(NSE)及 S100 β 蛋白水平的影响。方法:选取我院 2016 年 3 月~2017 年 3 月收治并择期行肺癌根治术治疗的 92 例患者,采取随机数字表法均分为两组。所有患者均采用相同的常规静吸复合麻醉,于麻醉诱导前 15 min(T_1)静脉滴注负荷剂量为 1 $\mu\text{g}/\text{kg}$ 的 Dex。观察组在此基础上以 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ 速度持续静脉泵注 Dex 至术前 10 min,对照组以等剂量生理盐水重复以上操作。记录比较两组 T_1 、单肺通气前(T_2)、单肺通气 60 min(T_3)、术毕时刻(T_4)、术后 24 h(T_5)血清 IL-6、NSE、S100 β 蛋白水平及术后不良反应的发生情况。结果:与 T_1 时间点对比,两组 T_2 、 T_3 、 T_4 、 T_5 时血清 IL-6、NSE、S100 β 水平均显著升高($P<0.01$),且观察组在 T_2 、 T_3 、 T_4 、 T_5 时血清 IL-6、S100 β 水平显著低于对照组同时($P<0.01$)。观察组术后不良反应率较对照组低($P<0.05$)。结论:肺癌根治术应用 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ 维持剂量右美托咪定(Dex)辅助麻醉更能有效降低术患者 IL-6、NSE、S100 β 蛋白水平,抑制机体炎症反应,减轻脑损伤,且安全性高。

关键词:肺癌根治术;右美托咪定;白细胞介素;神经元特异性烯醇化酶;S100 β 蛋白

中图分类号:R734.2 文献标识码:A 文章编号:1673-6273(2018)03-477-04

Effects of 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ Dose of Dexmedetomidine on the serum IL-6, NSE and S100 β Protein Levels of Patients with Lung Cancer Radical Surgery*

LING Hua¹, LIU Bin^{1△}, LIANG Xiao¹, XIE Xian-feng², XIE Ke-yu², SUN Yan²

(1 Department of Anesthesiology, West China Hospital, Sichuan University, Sichuan, Chengdu, 610041, China;

2 Department of Anesthesiology, the second people's Hospital of Chengdu, Sichuan, Chengdu, 610017, China)

ABSTRACT Objective: To explore the effect of 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ maintenance dose of dexmedetomidine (Dex) on the serum interleukin IL-6 (IL-6), neuron-specific enolase (NSE) and S100 β protein levels of patients with lung cancer radical surgery. **Methods:** 92 cases of patients undergoing elective resection of lung cancer treatment in our hospital from March 2016 to March 2017 were selected as research objectives and randomly divided into two groups. All cases were provided with the same conventional intravenous combined anesthesia, Dex was administered at a dose of 1 $\mu\text{g}/\text{kg}$ intravenously at 15 min before induction of anesthesia (T_1). The observation group was given continuous intravenous injection of Dex at a rate of 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ till 10 mins before operation, the above procedure was repeated with equal dose of saline to the control group. The serum IL-6, NSE, S100 β levels at T_1 , before single lung ventilation (T_2), single lung ventilation (T_3), operation finished time (T_4), postoperative 24 h (T_5) as well as the incidence of postoperative adverse reaction were compared between two groups. **Results:** The serum IL-6, NSE and S100 β protein levels at T_2 , T_3 , T_4 , T_5 were significant higher than those at T_1 ($P<0.01$), which were significantly lower in the observation group than those of the control group at same time points ($P<0.01$). The incidence of postoperative adverse reactions in observation group was significantly lower than that of the control group ($P<0.05$). **Conclusion:** 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ maintenance dose of Dex assisted anesthesia helps patient to reduce the serum IL-6, NSE, S100 β protein levels inhibiting the inflammatory response and reduce brain damage WITH high safely.

Key words: Lung cancer radical surgery; Dexmedetomidine; Interleukin-6; Neuron-specific enolase; S100 β protein

Chinese Library Classification(CLC): R734.2 **Document code:** A

Article ID: 1673-6273(2018)03-477-04

前言

肺癌根治术是近年来临床应用最为广泛的肺癌切除术式,

为非小细胞肺癌的首选治疗方法,其可彻底切除肺部原发肿瘤病灶,尽可能保留健康的肺组织^[1]。但在手术过程中气管插管、麻醉药物、手术操作均可在不同程度上引发机体产生应激与炎

* 基金项目:四川省卫生厅基金项目(080218)

作者简介:凌华(1978-),男,本科,主治医师,研究方向:麻醉科, E-mail: 993866070@qq.com, 电话: 15313116292

△ 通讯作者:刘斌,麻醉学博士研究生导师,副主任, E-mail: liubinhx@foxmail.com

(收稿日期:2017-06-29 接受日期:2017-07-25)

症反应,从而影响手术质量^[2]。为最大限制度地降低肺癌根治术手术创伤应激对患者机体造成的伤害,提高手术质量,临床须制定出更为有效、合理的麻醉方案。静吸复合麻醉是目前应用较为普遍的全身麻醉(general anesthesia,GA)方式,其特点是麻醉诱导快、麻醉深度可控性较强^[3]。右美托咪定(Dexmedetomidine,Dex)属 α_2 -肾上腺素受体(α_2 -adrenergic receptor, α_2 -AR)激动剂,具有抗交感神经、抗焦虑、镇静镇痛等作用,现已大量应用于全麻手术中^[4,5]。近年来有研究^[6]显示 Dex 还具有抗炎作用。本研究主要探讨了肺癌根治术应用 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ 维持剂量 Dex 辅助麻醉对患者白细胞介素(interleukin,IL-6)、神经元特异性烯醇化酶(neuron-specific enolase,NSE)、S100 β 蛋白水平的影响,以期对肺癌根治术麻醉管理提供参考依据。现报道如下。

1 资料与方法

1.1 一般资料

选取我院 2016 年 3 月~2017 年 3 月收治并择期行肺癌根

治术治疗的 92 例患者,采取随机数字表法均分为两组。纳入标准:① 年龄 18~60 岁;② 无麻醉禁忌证,美国麻醉医师协会(ASA)分级为 I~II 级^[7];③ 无肺癌根治术禁忌证,手术均顺利完成;④ 身体质量指数(BMI) $\leq 30 \text{ kg/m}^2$;⑤ 单肺通气时间 $\leq 150 \text{ min}$,手术时间 $\leq 200 \text{ min}$,机械通气时间 $<180 \text{ min}$,术中输血量 $<2000 \text{ mL}$;⑥ 未接受化疗、放疗;⑦ 自愿受试,签署知情同意书;⑧ 近期未有镇痛药、镇静剂、 β 受体阻滞剂等有关药物应用史;⑨ 临床资料完整。排除标准:① 既往有精神病、代谢性疾病、慢性疼痛、肾脏病等病史者;② 术前明显紧张焦虑者;③ 合并呼吸系统疾病(如肺结核、支气管炎、哮喘病等)、心脏病(如心肌炎、高血压性心脏病、心动过缓、风湿性心脏病等)、糖尿病、高血压等疾患者;④ 既往有麻醉镇痛药物滥用史者;⑤ 伴有凝血功能、肝功能障碍者;⑥ 过敏体质或对本研究药物过敏者;⑦ 哺乳或妊娠期妇女;⑧ 既往有嗜酒等不良习惯者。本研究经我院医学伦理委员会审查同意。两组基线资料、手术情况对比差异均无统计学意义($P>0.05$),具有临床可比性。见表 1~2。

表 1 两组基线资料的比较

Table 1 Comparison of the baseline information between two groups

Groups	n	Age(year)	Sex(case)		BMI(kg/m ²)	ASA classification(case)	
			Male	Female		Grade I	Grade II
Observation group	46	43.5 $\pm$ 6.1	24	22	24.1 $\pm$ 3.3	24	22
Control group	46	44.1 $\pm$ 6.3	25	21	24.5 $\pm$ 3.0	21	25
P		0.644	0.835		0.545	0.532	

表 2 两组手术情况比较

Table 2 Comparison of the operation situation between two groups

Groups	n	Operation time(min)	One lung ventilation	Mechanical	Total blood loss	Total infusion
			time(min)	ventilation time(min)	(mL)	volume(mL)
Observation group	46	186.3 $\pm$ 20.5	131.4 $\pm$ 20.3	162.3 $\pm$ 18.4	284.2 $\pm$ 15.8	1580.1 $\pm$ 98.7
Control group	46	187.1 $\pm$ 21.0	130.9 $\pm$ 19.8	163.1 $\pm$ 18.1	282.9 $\pm$ 16.2	1550.4 $\pm$ 95.8
P		0.853	0.905	0.834	0.698	0.147

1.2 麻醉方法

两组患者均给予一致的常规静吸复合麻醉,具体如下:1) 所有患者均给予相同的术前准备,入室后建立外周静脉通路(PVC),常规监测脉搏血氧饱和度(SpO_2)、心电图(ECG)、心率(HR)、中心静脉压(CVP)、平均动脉压(MAP)、气道峰压(Ppeak)等。于麻醉诱导前 15 min,将负荷剂量为 1 $\mu\text{g/kg}$ 的 Dex(江苏恩华药业股份有限公司,国药准字 H20110086)以静脉滴注的方式输注 10 min。2) 麻醉诱导:① 用药方案:舒芬太尼(0.5 $\mu\text{g/kg}$) + 咪达唑仑(0.03 mg/kg) + 维库溴铵(0.1 mg/kg) + 依托咪酯(0.3 mg/kg),静脉输注;② 患者均于满意的肌松条件与麻醉深度(BIS 为 50~55)下行气管插管,利用纤维支气管镜确定双腔位置,妥善固定后连接麻醉机;③ 设置参数:吸呼比为 1:1.5,氧流量 2 L/min,吸入氧浓度(FiO_2)100%,呼吸频率(RR)12 次/min, $\text{SpO}_2 > 90\%$,潮气量(VT)6~7 mL/Kg,呼气末二氧化碳分压(P_{ETCO_2})为 30~40 mmHg(1 mmHg=0.133 kPa)。3) 麻醉维持:① 用药方案:异丙酚(300~500 mg/h) + 瑞芬太尼(400~600 $\mu\text{g/h}$),

静脉输注,可间断静脉推注适量顺阿曲库铵;② 术中输液维持 5 mL/(kg·h),并给予琥珀酰明胶注射液和复方电解质 1:1 补充。

观察组:在此基础上,以 0.5 $\mu\text{g}(\text{kg}\cdot\text{h})$ 速度持续静脉泵注 Dex 至手术结束前 10 min。对照组:以等剂量生理盐水重复以上操作。

1.3 观察指标

1.3.1 血清 IL-6、NSE、S100 β 水平的测定 所有患者均于麻醉诱导前 15 min (T_1)、单肺通气前(T_2)、单肺通气 60 min(T_3)、术毕时刻(T_4)、术后 24 h(T_5)各抽取 6 mL/次的肘静脉血,离心分离血清,保存于 -80℃ 冰箱中待检;IL-6、NSE、S100 β 蛋白均运用酶联免疫法检测,仪器采用全自动酶标仪(美国伯乐,型号 680),试剂盒均购自德国 Roche 公司;上述各指标检测步骤均严格参照配套说明书执行。

1.3.2 术后不良反应的发生情况 对术后每位患者因麻醉药物而引起的不良反应(如恶心呕吐、呼吸抑制、寒战、躁动等)进行详细记录。

1.4 统计学分析

运用统计软件 SPSS19.0 分析处理数据, 计量资料以($\bar{x} \pm s$)表示, 应用 t 检验, 计数资料以(%)表示, 采用 χ^2 检验, 以 $P < 0.05$ 为差异有统计学意义。

2 结果

表 3 两组 T₁、T₂、T₃、T₄、T₅ 时血清 IL-6 水平的比较($\bar{x} \pm s$, ng/L)

Table 3 Comparison of the serum IL-6 level between two groups at T₁, T₂, T₃, T₄ and T₅ ($\bar{x} \pm s$, ng/L)

Groups	n	T ₁	T ₂	T ₃	T ₄	T ₅
Observation group	46	11.8 ± 4.3	18.8 ± 6.1* [#]	36.7 ± 7.9* [#]	75.8 ± 10.4* [#]	20.8 ± 7.4* [#]
Control group	46	12.1 ± 4.4	24.5 ± 6.3*	52.1 ± 8.4*	104.5 ± 11.3*	32.4 ± 9.4*

Note: Compared with T₁ in the same group, * $P < 0.01$; Compared with the same period, [#] $P < 0.01$.

2.2 两组不同时间点血清 NSE 水平的比较

与 T₁ 时间点对比, 两组 T₂、T₃、T₄、T₅ 时血清 NSE 水平均显

2.1 两组麻醉前后不同时间点血清 IL-6 水平的比较

与 T₁ 时间点对比, 两组 T₂、T₃、T₄、T₅ 时血清 IL-6 水平均显著升高($P < 0.01$), 且观察组在 T₂、T₃、T₄、T₅ 时血清 IL-6 水平均显著低于对照组同时($P < 0.01$), 见表 3。

著升高($P < 0.01$), 且观察组在 T₂、T₃、T₄、T₅ 时血清 NSE 水平显著低于对照组同时($P < 0.01$), 见表 4。

表 4 两组 T₁、T₂、T₃、T₄、T₅ 时血清 NSE 水平的比较($\bar{x} \pm s$, μg/L)

Table 4 Comparison of the serum NSE level between two groups at T₁, T₂, T₃, T₄ and T₅ ($\bar{x} \pm s$, μg/L)

Groups	n	T ₁	T ₂	T ₃	T ₄	T ₅
Observation group	46	8.5 ± 2.3	14.1 ± 3.3* [#]	19.4 ± 4.5* [#]	26.1 ± 6.8* [#]	13.2 ± 3.5* [#]
Control group	46	8.6 ± 2.5	20.4 ± 4.0*	25.5 ± 5.6*	31.8 ± 10.1*	18.9 ± 4.1*

Note: Compared with T₁ in the same group, * $P < 0.01$; Compared with the same period, [#] $P < 0.01$.

2.3 两组不同时间点血清 S100β 蛋白水平的比较

与 T₁ 时间点对比, 两组 T₂、T₃、T₄、T₅ 时血清 S100β 蛋白水

平均显著升高($P < 0.01$), 且观察组在 T₂、T₃、T₄、T₅ 时血清 S100β 蛋白水平显著低于对照组同时($P < 0.01$), 见表 5。

表 5 两组 T₁、T₂、T₃、T₄、T₅ 时血清 S100β 蛋白水平的比较($\bar{x} \pm s$, μg/mL)

Table 5 Comparison of the serum S100β level between two groups at T₁, T₂, T₃, T₄ and T₅ ($\bar{x} \pm s$, μg/mL)

Groups	n	T ₁	T ₂	T ₃	T ₄	T ₅
Observation group	46	0.17 ± 0.07	0.27 ± 0.10* [#]	1.15 ± 0.46* [#]	1.71 ± 0.74* [#]	1.05 ± 0.43* [#]
Control group	46	0.18 ± 0.07	0.38 ± 0.12	1.56 ± 0.57*	2.03 ± 0.97*	1.51 ± 0.55*

Note: Compared with T₁ in the same group, * $P < 0.01$; Compared with the same period, [#] $P < 0.01$.

2.4 两组术后不良反应发生情况的比较

观察组在术后出现 1 例恶心呕吐, 1 例心动过缓, 1 例躁动; 对照组出现 2 例呼吸抑制, 4 例恶心呕吐, 4 例躁动, 2 例心动过缓。观察组不良反应率为 6.5%(3/46), 较对照组【26.1%(12/46)】相比明显降低($P = 0.011$)。

3 讨论

肺癌根治术中, 气管插管、拔管等操作均可对患者机体产生强烈的刺激, 尤其是拔管时应激反应十分剧烈, 患者极易出现呕吐反射、躁动、呛咳反射等不适反应, 引发心律失常、BP 升高、HR 加快, 并可引发神经内分泌系统功能发生明显变化, 更甚者可出现脑血管意外、心搏停止等不良事件^[8,9]。肺癌根治术对患者创伤较大, 且单肺通气为肺癌根治术的必要环节, 易发生低氧血症, 引发肺部缺血再灌注, 造成生理功能紊乱。另外, 单肺通气的过度机械牵张刺激可引发各种炎性介质表达水平上调, 引发机体炎性反应^[10]。为此, 在肺癌根治术中应选择较为理想的麻醉管理方案(既能保证麻醉质量, 又可避免因麻醉过浅所致的严重并发症及麻醉过深而引发的苏醒延迟等)以减轻应激源对病人机体的损伤、提高手术安全性^[11,12]。

Dex 属镇静催眠药, 具有抗焦虑、镇痛、镇静等作用, 对 α₂-AR 具有高选择性, 可降低在应激状态下血压的异常升高和心率的异常增快, 降低心肌耗氧量, 稳定血液血流动力学且对呼吸无明显抑制作用。当前, Dex 已作为辅助用药广泛应用于重症监护病人和行 GA 手术患者机械通气与气管插管时的镇静。文献指出^[13]Dex 的药代动力学特性为静滴后分布半衰期($t_{1/2\alpha}$)约为 6min、消除半衰期($t_{1/2\beta}$)约为 2 h、稳态分布容积(V_{dss})约为 118L、起效时间约为 10~15 min。鉴于 Dex 的起效时间, 本研究 Dex 的应用时机定于麻醉诱导前 15 min。研究^[14,15]显示 Dex 的镇静镇痛效果具有一定剂量依赖性。临床上多应用 0.3 μg/(kg·h) 和 0.5 μg/(kg·h) 这两种维持剂量。王永祥等^[16]研究发现肺癌根治术患者麻醉维持阶段采用小剂量 [0.3 μg/(kg·h)] Dex 和大剂量 [0.8 μg/(kg·h)] Dex 辅助麻醉时不利于降低炎症指标和术后认知功能的恢复, 但中剂量 [0.5 μg/(kg·h)] Dex 既能维持合适的镇静深度, 又能有效降低术中炎症反应, 提高手术质量。曹刚等^[17]研究指出在肺癌根治术诱导前 10 min 内将 1 μg/kg 负荷剂量的 Dex 以静脉泵入后再续以 0.5 μg/(kg·h) 持续泵入辅助麻醉能有效抑制病人围术期应激反应。由此可见, 本研究制定的辅助麻醉方案 [麻醉诱导前 15 min 采取 Dex (1

μg/kg)静脉滴注 + 麻醉维持阶段以 0.5 μg/(kg·h)静脉持续泵注]是有一定理论与实践基础的。

IL-6 属趋化因子家族成员之一,是炎症反应中重要的促炎性细胞因子,具有急性期反应、调节免疫应答等多种生物效应,参与免疫应答和炎症反应,其机体含量能反映组织损伤程度^[18,19]。本研究结果显示:与本组 T₁ 相比,两组 T₂~T₅ 血清 IL-6 水平均显著升高,且观察组血清 IL-6 水平显著低于对照组同时,说明采用 0.5μg(kg·h)维持剂量 Dex 辅助麻醉方案更有助于减轻肺癌根治术患者机体炎症反应。分析原因可能为 Dex 持续抑制儿茶酚胺等介质释放,降低促炎性细胞因子的能力,发挥抗炎作用^[20-22]。NSE 为烯醇化酶的二聚体同工酶,可作为神经元的标志酶,其特异性存在于神经内分泌细胞和神经元中。研究发现在正常人体中血液 NSE 含量较低,而当血脑屏障被破坏或神经元受损破裂时,NSE 可通过血脑屏障进入血液,使血液中 NSE 水平升高^[23,24]。本研究结果显示:与本组 T₁ 相比,两组 T₂~T₅ 时间点血清 NSE 水平均显著升高,且观察组血清 NSE 水平显著低于对照组同时,提示肺癌根治术患者采用 0.5 μg (kg·h)维持剂量 Dex 辅助麻醉可降低血清 NSE 水平。究其原因可能与 Dex 能长效减少去甲肾上腺素(NE)合成与释放,从而起到良好的脑保护作用^[25]。S100β 蛋白是一种酸性钙离子结合蛋白,主要存在于雪旺细胞和神经胶质细胞中,具有调节能量代谢、细胞生长及参与胞内信号传导的功能,可协助背根神经元、皮层神经元、运动神经元的生长^[26,27]。在正常成人血清中,S100β 蛋白水平较低,不易被检测出,而在发生颅脑损伤的患者血清中,S100β 蛋白水平会显著升高^[28-30]。本研究结果显示:与本组 T₁ 相比,两组 T₂~T₅ 时间点血清 S100β 蛋白水平均显著升高,且观察组血清 S100β 蛋白水平显著低于对照组同时;提示肺癌根治术患者采用该辅助麻醉方案更能有效降低血清 S100β 蛋白的表达,保护脑组织。另外,从术后不良反应的角度分析,本研究结果显示:与对照组(26.1%)相比,观察组术后不良反应率仅为 6.5%,明显下降,且未见严重不良反应/事件。可见,该 Dex 辅助麻醉方案是安全有效的。

综上所述,应用 0.5 μg(kg·h)维持剂量右美托咪定辅助麻醉更能有效降低肺癌根治术患者血清 IL-6、NSE、S100β 蛋白水平,具有一定的脑保护作用。但对于右美托咪定辅助麻醉方案的具体作用机制及有效性、安全性,仍应开展更多临床研究进一步论证与分析。

参考文献(References)

- [1] Wang W, Peng G, Guo Z, et al. Radical resection of right upper lung cancer using uniportal video-assisted thoracic surgery with non-intubated anesthesia[J]. J Thorac Dis, 2016, 7(12): 2362-2365
- [2] Aokage K, Yoshida J, Hishida T, et al. Limited resection for early-stage non-small cell lung cancer as function-preserving radical surgery: a review[J]. Jpn J Clin Oncol, 2016, 47(1): 7
- [3] Dongchun Ma J T X J. Radical resection of right upper lung under complete video-assisted thoracoscopic surgery[J]. J Thorac Dis, 2013, 5(Suppl 3): S291
- [4] Akin A, Bayram A, Esmoğlu A, et al. Dexmedetomidine vs midazolam for premedication of pediatric patients undergoing anesthesia[J]. Pediatr Anesth, 2012, 22(9): 871-876
- [5] Zhang X Y, Liu Z M, Wen S H, et al. Dexmedetomidine administration before, but not after, ischemia attenuates intestinal injury induced by intestinal ischemia-reperfusion in rats [J]. Anesthesiology, 2012, 116(5): 1035
- [6] Li B, Li Y, Tian S, et al. Anti-inflammatory Effects of Perioperative Dexmedetomidine Administered as an Adjunct to General Anesthesia: A Meta-analysis[J]. Sci Rep, 2015, 5(9): 12342
- [7] Koo C Y, Hyder J A, Wanderer J P, et al. A meta-analysis of the predictive accuracy of postoperative mortality using the American Society of Anesthesiologists' physical status classification system [J]. World J Surg, 2015, 39(1): 88-103
- [8] Okada M. Radical sublobar resection for small-diameter lung cancers [J]. Thorac Surg Clin, 2013, 23(3): 301-311
- [9] Jiang H G, Li J, Shi S B, et al. Value of fibrinogen and D-dimer in predicting recurrence and metastasis after radical surgery for non-small cell lung cancer[J]. Med Oncol, 2014, 31(7): 1-9
- [10] Pompili C. Quality of life after lung resection for lung cancer [J]. J Thorac Dis, 2015, 7(Suppl 2): S138
- [11] Schlijper R C J, Grutters J P C, Houben R, et al. What to choose as radical local treatment for lung metastases from colo-rectal cancer: Surgery or radiofrequency ablation?[J]. Cancer Treat Rev, 2014, 40(1): 60-67
- [12] Zhao J, Zhao Y, Xuan Y, et al. Prognostic impact of CUG-binding protein 1 expression and vascular invasion after radical surgery for stage IBnon-small cell lung cancer[J]. Indian J Cancer, 2015, 52 Suppl 2(6): e125
- [13] Djaiani G, Silverton N, Fedorko L, et al. Dexmedetomidine versus Propofol Sedation Reduces Delirium after Cardiac Surgery: A Randomized Controlled Trial[J]. Anesthesiology, 2016, 124(2): 362-368
- [14] Hsu Y W, Cortinez L I, Robertson K M, et al. Dexmedetomidine Pharmacodynamics: Part I- Crossover comparison of the respiratory effects of dexmedetomidine and remifentanyl in healthy volunteers[J]. Anesthesiology, 2004, 101(5): 1066-1076
- [15] Behmenburg F, Pickert E, Mathes A, et al. The Cardioprotective Effect of Dexmedetomidine in Rats Is Dose-Dependent and Mediated by BKCa Channels[J]. J Cardiovasc Pharmacol, 2017, 69(4): 228-235
- [16] Wang Y X, Cao J F. Effect of Different Dose of Dexmedetomidine on Postoperative Cognitive Function of Lung Cancer Patients Treated with Radical Resection[J]. Pract J Cancer, 2015, 30(11): 1646-1648
- [17] Cao G, Zhu H, Huang Z S. Effects of dexmedetomidine on perioperative pulmonary shunt fraction and inflammatory reactions in patients with pulmonary cancer[J]. Chin J Hosp Pharm, 2015, 35(9): 822-824
- [18] Farghaly H S, Mahmoud A M, Abdel-Sater K A. Effect of dexmedetomidine and cold stress in a rat model of neuropathic pain: role of interleukin-6 and tumor necrosis factor-α [J]. Eur J Pharmacol, 2016, 776(19): 139-145
- [19] Tanabe K, Matsushima-Nishiwaki R, Kozawa O, et al. Dexmedetomidine suppresses interleukin-1β-induced interleukin-6 synthesis in rat glial cells[J]. Int J Mol Med, 2014, 34(4): 1032-1038
- [20] Song L, Smith M A, Doshi P, et al. Antitumor efficacy of the anti-interleukin-6 (IL-6) antibody siltuximab in mouse xenograft models of lung cancer[J]. J Thoracic Oncol, 2014, 9(7): 974-982

- Foundation, 2016, 24(4): 252-258
 - [13] Wollert KC, Kempf T. Growth Differentiation Factor 15 as a Biomarker in Cardiovascular Disease[J]. Clinical chemistry, 2017, 63(1): 140-151
 - [14] Zhang M, Pan K, Liu Q, et al. Growth differentiation factor 15 may protect the myocardium from no reflow by inhibiting the inflammatory like response that predominantly involves neutrophil infiltration[J]. Molecular medicine reports, 2016, 13(1): 623-632
 - [15] Kempf T, Zarbock A, Widera C, et al. GDF-15 is an inhibitor of leukocyte integrin activation required for survival after myocardial infarction in mice[J]. Nature medicine, 2011, 17(5): 581-588
 - [16] Kempf T, Horn-Wichmann R, Brabant G, et al. Circulating concentrations of growth-differentiation factor 15 in apparently healthy elderly individuals and patients with chronic heart failure as assessed by a new immunoradiometric sandwich assay [J]. Clinical chemistry, 2007, 53(2): 284-291
 - [17] Nair V, Robinson-Cohen C, Smith MR, et al. Growth Differentiation Factor-15 and Risk of CKD Progression [J]. JASN, 2017, 28(7): 2233-2240
 - [18] Kahli A, Guenancia C, Zeller M, et al. Growth differentiation factor-15 (GDF-15) levels are associated with cardiac and renal injury in patients undergoing coronary artery bypass grafting with cardiopulmonary bypass[J]. PloS one, 2014, 9(8): e105759
 - [19] Abulizi P, Loganathan N, Zhao D, et al. Growth Differentiation Factor-15 Deficiency Augments Inflammatory Response and Exacerbates Septic Heart and Renal Injury Induced by Lipopolysaccharide[J]. Scientific reports, 2017, 7(1): 1037
 - [20] Mazagova M, Buikema H, Van Buiten A, et al. Genetic deletion of growth differentiation factor 15 augments renal damage in both type 1 and type 2 models of diabetes [J]. American journal of physiology Renal physiology, 2013, 305(9): F1249-64
 - [21] Ju W, Nair V, Smith S, et al. Tissue transcriptome-driven identification of epidermal growth factor as a chronic kidney disease biomarker [J]. Science translational medicine, 2015, 7(316): 316ra193
 - [22] Martini S, Nair V, Keller BJ, et al. Integrative biology identifies shared transcriptional networks in CKD [J]. JASN, 2014, 25(11): 2559-2572
 - [23] Roshanravan B, Khatri M, Robinson-Cohen C, et al. A prospective study of frailty in nephrology-referred patients with CKD [J]. American journal of kidney diseases: the official journal of the National Kidney Foundation, 2012, 60(6): 912-921
 - [24] Roshanravan B, Robinson-Cohen C, Patel KV, et al. Association between physical performance and all-cause mortality in CKD [J]. JASN, 2013, 24(5): 822-830
 - [25] Breit SN, Carrero JJ, Tsai VW, et al. Macrophage inhibitory cytokine-1 (MIC-1/GDF15) and mortality in end-stage renal disease[J]. Nephrol Dial Transplan, 2012, 27(1): 70-75
-
- (上接第 480 页)
- [21] Lee S O, Yang X, Duan S, et al. IL-6 promotes growth and epithelial-mesenchymal transition of CD133+ cells of non-small cell lung cancer[J]. Oncotarget, 2015, 7(6): 6626
 - [22] Shams T, Bahnasawe N S E, Abusamra M, et al. Induced hypotension for functional endoscopic sinus surgery: A comparative study of dexmedetomidine versus esmolol [J]. Saudi J Anaesth, 2013, 7(2): 175-180
 - [23] Dutta S, Karol M D, Cohen T, et al. Effect of dexmedetomidine on propofol requirements in healthy subjects [J]. J Pharm Sci, 2015, 90(2): 172-181
 - [24] Calderon L M, Guyette F X, Doshi A A, et al. Combining NSE and S100B with clinical examination findings to predict survival after resuscitation from cardiac arrest[J]. Resuscitation, 2014, 85(8): 1025
 - [25] Zhao J, Zhou C. The protective and hemodynamic effects of dexmedetomidine on hypertensive cerebral hemorrhage patients in the perioperative period[J]. Exp Ther Med, 2016, 12(5): 2903-2908
 - [26] Mazzone G L, Nistri A. S100 β as an early biomarker of excitotoxic damage in spinal cord organotypic cultures [J]. J Neurochemistry, 2014, 130(4): 598
 - [27] Qin B, Panickar K S, Anderson R A. Cinnamon polyphenols regulate S100 β , sirtuins, and neuroactive proteins in rat C6 glioma cells[J]. Nutrition, 2014, 30(2): 210-217
 - [28] Zhao L H, Shi Z H, Yin N N, et al. Use of dexmedetomidine for prophylactic analgesia and sedation in delayed extubation patients after craniotomy: a study protocol and statistical analysis plan for a randomized controlled trial[J]. Trials, 2013, 14(1): 1-6
 - [29] Liu Xian-bao, Zhan Hong, Zeng Xu, et al. Dexmedetomidine Reduced Cytokine Release during Postpartum Bleeding-Induced Multiple Organ Dysfunction Syndrome in Rats [J]. Mediators Inflamm, 2013, 2013(2): 627831
 - [30] Qin B, Panickar K S, Anderson R A. Cinnamon polyphenols attenuate the hydrogen peroxide-induced down regulation of S100 β secretion by regulating sirtuin 1 in C6 rat glioma cells [J]. Life Sci, 2014, 102(1): 72-79