doi: 10.13241/j.cnki.pmb.2014.09.026

全身麻醉和硬膜外麻醉对老年骨科手术患者术后短期认知功能的影响

莫桂熙 刘奕君 莫 坚 梁广彬 张良清

(广东医学院附属医院麻醉科 广东 湛江 524001)

摘要 目的:探讨全身麻醉和硬膜外麻醉对老年骨科手术患者术后短期认知功能的影响。**方法:**按随机数字方式将2010年3月至2013年5月收治的全麻骨科手术老年患者64例分为两组,全身麻醉组(32例)给予全身麻醉进行手术,硬膜外麻醉组(32例)给予硬膜外麻醉进行手术,对比分析两组观察麻醉前后动脉血压与心率,睁眼、拔管及应答时间,术后6、12、24、72 h的MMSE评分差异,并统计术后POCD的发生情况。**结果:**两组的年龄、体重、麻醉时间、受教育时间、出血量等一般临床资料均无明显差异(P>0.05);两组麻醉前、麻醉后术前、手术0.5h及手术结束时动脉血压和心率差异均不显著(P>0.05);全身麻醉组的睁眼、拔管及应答时间分别为(30.3±10.5)min、(30.3±7.8)min、(33.2±9.6)min;膜外麻醉组的睁眼、拔管及应答时间分别为(30.6±11.6)min、(30.1±6.6)min、(34.3±8.5)min,两组差异不显著(P>0.05);全身麻醉组麻醉前MMSE评分为29.2±1.5,而膜外麻醉组麻醉前MMSE评分为29.1±1.0,差异不显著(P>0.05);麻醉后,两组的MMSE评分均出现先减少后恢复的变化,膜外麻醉组麻醉后24h时的MMSE评分28.7±1.0明显高于全身麻醉组的27.3±0.8(t=5.491,P=0.000<0.05);全身麻醉组麻醉后6h和12hPOCD的发生率均明显高于膜外麻醉组的(P<0.05),而两组在麻醉后24h开始POCD的发生率无明显差异(P>0.05)。**结论:**全身麻醉对老年骨科手术患者术后短期认知功能的影响明显大于硬膜外麻醉。

关键词:全身麻醉;硬膜外麻醉;术后认知功能障碍;认知功能

中图分类号:R614,R68 **文献标识码:**A **文章编号:**1673-6273(2014)09-1704-05

Postoperative Short-term Cognitive Function in Elderly Orthopedic Patients Treating with General Anesthesia and Epidural Anesthesia

MO Gui-xi, LIU Yi-jun, MO Jian, LIANG Guang-bin, ZHANG Liang-qing

(Department of anesthesiology, Affiliated Hospital of Guangdong Medical College, Zhanjiang, Guangdong, 524001, China)

ABSTRACT Objective: To study the postoperative short-term cognitive function of the general anesthesia and epidural anesthesia in elderly patients with the orthopedic disease. **Methods:** 64 elderly patients March 2010 to May 2013 with general anesthesia were divided into two groups by way of random Numbers, the general anesthesia group (32 cases) were given general anesthesia surgery, epidural anesthesia group (32 cases) were given epidural anesthesia surgery, before and after anesthesia arterial blood pressure and heart rate, the time of open, tube drawing and reply, the MMSE score of postoperative 6, 12, 24, 72 h were contrastively analysis. **Results:** two groups of age, weight, anesthesia time, education time, blood loss, such as general clinical data had no obvious difference (P>0.05); before anesthesia, after anesthesia preoperative, 0.5 h and surgery at the end of the arterial blood pressure and heart rate of two groups had significant difference (P>0.05); General anesthesia group open and tube drawing and response time, respectively were (30.3 ± 10.5) min and (30.3-7.8) min and (33.2 ± 9.6 min). Epidural anesthesia group open and tube drawing and response time (30.6± 11.6) min, respectively (30.1± 6.6) min and (34.3 ± 8.5) min, there were no significant differences between the two groups (P>0.05). General anesthesia group of MMSE score before anesthesia was 29.2 ± 1.5, anesthesia and epidural anesthesia group before the MMSE score was 29.1± 1.0, with no significant difference(P>0.05). After anesthesia, the two groups after the MMSE score of all appear to reduce the change of the recovery, 24 h after anesthesia epidural anesthesia group was significantly better than the MMSE score of 28.7± 1.0 of the general anesthesia group 27.3 ± 0.8 (t=5.491, P=0.000 <0.05); 6 h after anesthesia and general anesthesia group 12 hpocd incidence were significantly higher than that of epidural anesthesia group (P<0.05), and two groups began to the incidence of POCD in 24 h after anesthesia had no obvious difference (P>0.05). **Conclusion:** The effect of general anesthesia on postoperative short-term cognitive function in elderly patients with orthopaedic surgery significantly is greater than epidural anesthesia.

Key words: General anesthesia; Epidural anesthesia; Postoperative cognitive dysfunction; Cognitive function

Chinese Library Classification(CLC): R737.9 Document code: A

Article ID: 1673-6273(2014)09-1704-05

作者简介:莫桂熙(1980-),男,学士,主治医师,主要从事围术期器官保护方面的研究,E-mail:myseige@126.com

(收稿日期:2013-08-11 接受日期:2013-09-10)

前言

术后认知功能障碍(POCD)是一种手术后出现的中枢神经系统的并发症,即术后精神功能障碍,在老年人群中的发病率较高,临床主要表现为认知能力障碍、精神混乱、记忆受损及焦虑等[1-3]。目前对于术后精神障碍的机理尚不完善,可能涉及到中枢神经系统、内分泌和免疫系统的紊乱,一般认为,老年术后精神障碍是在中枢神经系统退化的基础上,由多种因素造成中枢神经递质系统的进一步紊乱所引起的急性精神紊乱综合征[4-5]。POCD 的持续时间可数月可数年,短期的主要表现为术后记忆力减退以及集中力降低的智力功能发生退化,本文探讨全身麻醉和硬膜外麻醉对老年骨科患者术后短期认知功能的影响,现将工作总结如下。

1 资料与方法

1.1 一般资料

对象均入选于 2010 年 3 月至 2013 年 5 月收治的全麻骨科手术老年患者 64 例, 所有患者均符合入选标准[6-8]: ①按 ASA 标准分级为 ASAⅠ、Ⅱ两级;②年龄均大于 64 岁;③排除肝病、中风、神经和精神系统疾病或服用相关药物的患者。按随机数字法将 64 例患者随机分为两组,全身麻醉组,32 例,其男 18 例,女 14 例,硬膜外麻醉组,32 例,男 20 例,女 12 例。

1.2 方法

在麻醉前 30min,所有患者给予 0.5mg 阿托品肌注,并对其生命体征进行监测,开放上肢静脉通路,给予 10 mL/min 的乳酸林格氏液静脉滴注。全身麻醉组:依次给予 0. 04mg/kg 咪达唑仑,5μg / kg 芬太尼,0.3 mg / kg 的依托咪酯和 1mg 维库溴铵静脉注射,待 3min 后,行气管插管,之后接麻醉呼吸机行机械通气。硬膜外麻醉组:患者平卧,在其 L1～2 间行硬膜外穿刺置管,给予 2%利多卡因 3 ml,并给予 0. 375%罗哌卡因 2 mL/次,至麻醉平面;若术中,患者血压小于 11.97/7. 98 kPa,需加注麻黄碱 6 mg/ 次;若心率低于 50,需加注麻黄碱 阿托品 0. 5 mg / 次。

1.3 观察指标

①记录两组的一般临床资料;②观察麻醉前、麻醉后术前、手术 0.5h 及手术结束时动脉血压与心率;③记录患者睁眼、拔管及应答时间;④并按照简易精神状况检测量表(MMSE) 评分评价两组术后 6、12、24、72 h 的精神状况。

1.4 统计学处理及分析

采用 SPSS15.0 软件统计分析,计量资料以($\bar{x}$ ± s)表示,差异性比较采用 t 检验, 计数资料采用 X^2 检验,P<0.05 差异显著,认为具有统计学意义。

2 结果

2.1 一般临床指标

两组的年龄、性别比、体重、麻醉时间、受教育时间、出血量等一般临床资料均无明显差异,P＞0.05, 无统计学院意义,具有可比性,见表 1。

表 1 两组一般临床资料对比

Table 1 Comparison of clinical data between two groups

指标 Indexes	全身麻醉组 General anesthesia group	膜外麻醉组 Epidural anesthesia group	T/X^2	P
例数 Cases	32	32	-	-
年龄(岁)Age(years)	69.3 ± 6.4	71.2 ± 5.3	1.293	0.100＞0.05
性别(男 / 女)Gender (male / female)	18/14	20/12	0.259	0.611＞0.05
体重(kg)Body weight (kg)	60.2 ± 4.8	61.3 ± 5.6	0.844	0.201＞0.05
麻醉时间(h)Time of anesthesia (H)	2.6 ± 0.2	2.7 ± 0.3	1.569	0.061＞0.05
受教育时间(年)Education time (years)	7.2 ± 1.2	7.4 ± 1.1	0.695	0.245＞0.05
出血量(ml)Amount of bleeding (ML)	308.4 ± 40.4	320.14 ± 58.2	0.937	0.176＞0.05

2.2 麻醉前后动脉血压和心率变化

两组麻醉前、麻醉后术前、手术 0.5h 及手术结束时动脉血压有微小的上升波动, 两组差异进行对比, 差异不显著,P＞0.05,无统计学院意义,见表 2。两组麻醉前、麻醉后术前、手术 0.5h 及手术结束时心率差异不显著,P＞0.05, 无统计学院意义,见表 3。

2.3 睁眼、拔管及应答时间

全身麻醉组的睁眼、拔管及应答时间分别为(30.3 ± 10.5)min、(30.3 ± 7.8)min、(33.2 ± 9.6)min; 膜外麻醉组的睁眼、拔管及应答时间分别为 (30.6 ± 11.6)min、(30.1± 6.6)min、(34.3 ± 8.5)min,两组差异不显著,P＞0.05,无统计学院意义,见表 4。

2.4 麻醉前后 MMSE 评分变化

全身麻醉组麻醉前 MMSE 评分为 29.2 ± 1.5,而膜外麻醉组麻醉前 MMSE 评分为 29.1 ± 1.0, 差异不显著,P＞0.05,无统计学院意义;麻醉后,两组的 MMSE 评分均出现先减少后恢复的变化,另外,在麻醉后 24h 时,膜外麻醉组的 MMSE 评分 28.7 ± 1.0 明显高于全身麻醉组的 27.3 ± 0.8,t=5.491,P=0.000<0.05,差异显著,具有统计学意义,其余无显著性差异,见表 5。

2.5 麻醉后 POCD 的发生情况

全身麻醉组麻醉后 6h 和 12h POCD 的发生率均明显高于膜外麻醉组的,P<0.05,差异显著,具有统计学意义;而两组在麻醉后 24h 开始 POCD 的发生率无明显差异,P＞0.05,见表 6。

表 2 两组麻醉前后动脉血压变化对比

Table 2 Changes of arterial blood pressure between two groups before and after anesthesia

指标 Indexes	全身麻醉组 General anesthesia group	膜外麻醉组 Epidural anesthesia group	t	P
例数 Cases	32	32	-	-
麻醉前 Before anesthesia	11.3 ± 0.5	11.2 ± 0.6	1.449	0.076＞0.05
麻醉后术前 After anesthesia and before the operation	11.3 ± 0.8	11.1 ± 0.6	1.131	0.131＞0.05
手术 0.5h 0.5h of operation	11.6 ± 0.7	11.4 ± 0.7	1.143	0.129＞0.05
手术结束时 End of operation	11.8 ± 1.0	11.9 ± 0.8	0.442	0.330＞0.05

表 3 两组的麻醉前后心率变化

Table 3 Changes of arterial heart rate between two groups before and after anesthesia

指标 Indexes	全身麻醉组 General anesthesia group	膜外麻醉组 Epidural anesthesia group	t	P
例数 Cases	32	32	-	-
麻醉前 Before anesthesia	85.4± 6.5	85.9± 7.1	0.294	0.385＞0.05
麻醉后术前 After anesthesia and before the operation	82.3± 4.5	82.8± 5.3	0.407	0.343＞0.05
手术 0.5h 0.5h of operation	85.7± 5.6	85.5± 6.1	0.137	0.446＞0.05
手术结束时 End of operation	83.5± 6.2	84.1± 5.7	0.403	0.344＞0.05

表 4 两组的睁眼、拔管及应答时间对比

Table 4 Comparison of eye opening, extubation and response time between two groups

指标 Indexes	全身麻醉组 General anesthesia group	膜外麻醉组 Epidural anesthesia group	t	P
例数 Cases	32	32	-	-
睁眼时间(min) Eye opening time(min)	30.3± 10.5	30.6± 11.6	0.108	0.457＞0.05
拔管时间(min) Extubation time(min)	30.3± 7.8	30.1± 6.6	0.111	0.456＞0.05
应答时间(min) Response time(min)	33.2± 9.6	34.3± 8.5	0.485	0.315＞0.05

表 5 两组麻醉前后 MMSE 评分对比

Table 5 Comparison of MMSE score between two groups before and after anesthesia

指标 Indexes		全身麻醉组 General anesthesia group	膜外麻醉组 Epidural anesthesia group	t	P
例数 Cases		32	32		
麻醉前 Before anesthesia		29.2± 1.5	29.1± 1.0	0.314	0.377＞0.05
麻醉后 After anesthesia	6h	26.6± 0.8	26.8± 0.6	1.131	0.131＞0.05
	12h	25.8± 0.8	25.5± 0.7	1.596	0.058＞0.05
	24h	27.3± 0.8	28.7± 1.0	5.491	0.000<0.0
	72h	29.3± 0.8	29.1± 0.9	0.940	0.176＞0.05

表 6 两组麻醉后 POCD 的发生情况对比

Table 6 Comparison of the incidence of POCD between two groups after anesthesia

指标 Indexes		全身麻醉组 General anesthesia group	膜外麻醉组 Epidural anesthesia group	X^2	P
例数 Cases		32	32	-	-
麻醉后 After anesthesia	6h	8(25.0)	2(6.3)	4.267	0.039
	12h	9(28.1)	2(6.3)	5.379	0.020
	24h	4(12.5)	3(9.4)	0.160	0.689
	72h	2(6.3)	1(3.1)	0.350	0.554

3 讨论

POCD 是术后人格、社交能力及认知能力和技巧的变化，即术后认知功能障碍，老年人手术后主要出现中枢神经系统并发症，表现为精神错乱、焦虑、人格的改变以及记忆受损[9-10]。近年来老年患者全麻术后 POCD 发生率一直居高不下，它使患者记忆力、语言能力、判断能力及工作能力丧失，渐渐已成了老年患者术后严重的并发症之一[11-12]。POCD 的发病机制可能与年龄、手术创伤、麻醉药物、疾病种类及应激反应等因素有关[13-16]。与麻醉药物有关系主要表现在麻醉方式，一直以来不同麻醉方法与 POCD 的关系存在很大争议。有研究[17]表明，全身麻醉 POCD 的发生率要低于椎管内麻醉以及局部麻醉患者，而近年来，相关研究报道，老年患者 POCD 与麻醉方式之间不存在显著的相关性，麻醉方式是其中一个独立预测因素[18,19]。本文研究中，全身麻醉组麻醉后 6h 和 12hPOCD 的发生率均明显高于膜外麻醉组的（P<0.05），而两组在麻醉后 24h 开始 POCD 的发生率无明显差异（P＞0.05），这提示在术后短期认知功能的对比中，全身麻醉的影响作用更大，之后，全身麻醉和膜外麻醉对患者术后认知功能的影响类似，不存在显著性差异。

本文研究显示，两组的年龄、体重、麻醉时间、受教育时间、出血量等一般临床资料均无明显差异（P＞0.05），这提示两组的临床资料类似，具有可比性。两组麻醉前、麻醉后术前、手术 0.5h 及手术结束时动脉血压和心率差异均不显著（P＞0.05），两组麻醉组的睁眼、拔管及应答时间分别为差异不显著（P＞0.05），这提示全身麻醉和膜外麻醉对手术中血压和心率等资料不存在明显差异，作用类似。老年患者自身机体各组织器官活性减弱，经骨科手术后，肢体出现疼痛，甚至长期卧床，不宜用长时间进出术后短期认知功能测试。因此，本文通过 MMSE 评分进行衡量，MMSE 量表具有简单易操作、时间短，有研究[20]证实，MMSE 评分与痴呆患者 CT 的脑萎缩程度呈正相关，非常适合用于大多数老年患者术后认知功能评价。全身麻醉组麻醉前 MMSE 评分为 29.2 ± 1.5，而膜外麻醉组麻醉前 MMSE 评分为 29.1 ± 1.0，差异不显著（P＞0.05）；麻醉后，两组的 MMSE 评分均出现先减少后恢复的变化，膜外麻醉组麻醉后 24h 时的 MMSE 评分 28.7± 1.0 明显高于全身麻醉组的 27.3 ± 0.8（t=5.491，P=0.000<0.05）；这进一步证实，全身麻醉对术后短期认知功能的影响作用更大，而之后，全身麻醉和膜外麻醉对患者术后认知功能的影响基本一样。

对于 POCD 的发生，目前最好的措施还是以预防为主。提高对该病的认识，通过术前心理教育进行心理精神治疗，利于诊断与治疗；术前做好患者身体状况的监测，及时评估患者的手术承受能力；合理用药，维持血压、营养、体液及电解质平衡；药物治疗时，注意药物的药性不影响老年人的认知能力，随时并严密监控血压、血氧和呼吸的饱和度；术后出现精神障碍健忘综合征及精神异常等，及时给予相应的措施治疗，缓解症状。总之，全身麻醉对老年骨科手术患者术后短期认知功能的影响明显大于硬膜外麻醉，因此针对临床实际情况，应积极采取相应的措施进行预防和治疗，将老年骨科手术患者 POCD 的发生率降到最低。

参考文献（References）

[1] 庞芸, 钟海星, 王强, 等. 乌司他丁对老年患者下肢关节置换术后认知功能障碍的影响[J]. 现代生物医学进展, 2013, 13(14):2726-2729
Pang Yun, Zhong Hai-xing, Wang Qiang, et al. Effects of Ulinastatin on Post-operative Cognitive Dysfunction in Elderly Patients with Lower Limb Joint Replacement Surgery[J]. Progress in Modern Biomedicine, 2013, 13(14):2726-2729

[2] Peng L, Xu L,Ouyang W. Role of Peripheral Inflammatory Markers in Postoperative Cognitive Dysfunction (POCD): A Meta-Analysis[J]. PloS one, 2013, 8(11): e79624

[3] Steinmetz J, Jespersgaard C, Dalhoff K, et al. Cytochrome P450 polymorphism and postoperative cognitive dysfunction[J]. Minerva anestesiologica, 2012, 78(3): 303

[4] Jungwirth B, Zieglgansberger W, Kochs E, et al. Anesthesia and postoperative cognitive dysfunction (POCD)[J]. Mini Reviews in Medicinal Chemistry, 2009, 9(14): 1568-1579

[5] Laalou F Z, Jochum D, Pain L. Postoperative cognitive dysfunction (POCD): strategy of prevention, assessment and management][C]//Annales fran aises d'anesthè sie et de rèanimation, 2011, 30(10): e49

[6] 胡楚文, 赵一凡, 王飞, 等. 右美托咪定预防骨科脊柱手术患者全麻后寒战的临床观察[J]. 临床麻醉学杂志, 2012, 28(1):34-36
Hu Chu-wen, Zhao Yi-fan,Wang Fei, et al. Dexmedetomidine prevent postoperative shivering in patients undergoing spinal surgery [J]. The Journal of Clinical Anesthesiology, 2012, 28(1):34-36

[7] 姚杰, 孟尽海, 王文娟, 等. 不同麻醉方法对骨科手术患者深静脉血栓形成的影响[J]. 宁夏医科大学学报, 2013, 35(1):29-31, 36
Yao Jie, Meng Jin-hai, Wang Wen-juan, et al. Effect of Different Anesthesia on Deep Venous Thrombosis after Orthopedic Surgery[J]. Journal of Ningxia Medical University, 2013, 35(1):29-31, 36

[8] 陈伟元, 王焕彬. 全麻和硬膜外麻醉对老年患者骨科手术后认知功能的影响[J]. 医学综述, 2013, 19(12):2274-2275

Chen Wei-yuan, Wang Huan-bin. Impact of General Anesthesia and Epidural Anesthesia on Short-term Cognitive Function in Elderly Patients after Orthopedic Surgery[J]. Medical Recapitulate, 2013, 19(12): 2274-2275

[9] Mu D L, Wang D X, Li L H, et al. Postoperative delirium is associated with cognitive dysfunction one week after coronary artery bypass grafting surgery [J]. Acta of Pecking Hniversity (Medical Science), 2011, 43(2): 242

[10] Funder K S, Steinmetz J, Rasmussen L S. Cognitive dysfunction after cardiovascular surgery[J]. Minerva anestesiologica, 2009,75(5): 329

[11] Bryson G L, Wyand A, Wozny D, et al. The clock drawing test is a poor screening tool for postoperative delirium and cognitive dysfunction after aortic repair[J]. Canadian Journal of Anesthesia/Jo urnal canadien d'anesthésie, 2011, 58(3): 267-274

[12] Cui Q T, Fu Q L, Han P L, et al. Risk factors of cognitive impairment after off-pump coronary artery bypass grafting [J]. China Jouinal of Cardiology, 2012, 40(2): 104

[13] 谭文斐, 赵芸慧, 方波, 等. 患者自控静脉镇痛引起术后认知功能障碍的病例对照研究[J].中华流行病学杂志, 2008, 29(2):188-190
Tan Wen-fei, Zhao Yun-hui, Fang Bo, et al. A case-control study on the risk factors in postoperative cognitive dysfunction induced by patient selfcontrolled intravenous analgesia [J]. Chinese Journal of Epidemiology, 2008, 29(2):188-190

[14] 陶伟萍, 毛巧燕, 杨建萍, 等. 脊柱手术患者家庭关怀度与术后认知功能障碍的相关性分析[J].中华行为医学与脑科学杂志, 2013, 22(10):908-910
Tao Wei-ping, Mao Qiao-yan, Yang Jian-ping, et al. The relationship between family care and postoperative cognitive dysfunction in patients undergoing spinal surgery[J]. Chinese Journal of Behavioral Medicine and Brain Science, 2013, 22(10):908-910

[15] Spiegel D R, Chen V. A Case of Postoperative Cognitive Decline, with a Highly Elevated C-Reactive Protein, Status Post Left Ventricular Assist Device Insertion: A Review of the Neuroinflammatory Hypothesis of Delirium[J]. Innovations in clinical neuroscience, 2012, 9(1): 35

[16] Hu Z, Ou Y, Duan K, et al. Inflammation: a bridge between postoperative cognitive dysfunction and Alzheimer's disease [J]. Medical hypotheses, 2010, 74(4): 722-724

[17] Seitz D, Shah P, Herrmann N, et al. Exposure to general anesthesia and risk of Alzheimer's disease: a systematic review and meta-analysis[J]. BMC geriatrics, 2011, 11(1): 83

[18] McDonagh D L, Mathew J P, White W D, et al. Cognitive function after major noncardiac surgery, apolipoprotein E4 genotype, and biomarkers of brain injury[J]. Anesthesiology, 2010, 112(4): 852

[19] 章放香, 宁俊平, 邱冰, 等. 不同麻醉老年患者术后认知功能障碍发生的比较[J]. 中华麻醉学杂志, 2013, 33(2):188-190
Zhang Fang-xiang, Ning Jun-ping, Qiu Bing, et al. Comparison of occurrence of postoperative cognitive dysfunction in elderly patients using different anesthetic methods[J]. Chinese Journal of Anesthesiology, 2013, 33(2):188-190

[20] Ballard C, Jones E, Gauge N, et al. Optimised anaesthesia to reduce post operative cognitive decline (POCD) in older patients undergoing elective surgery, a randomised controlled trial [J]. PloS one, 2012,7 (6): e37410

(上接第 1771 页)

[26] Bachnoff N, Trus M, Atlas D. Alleviation of oxidative stress by potent and selective thioredoxin-mimetic peptides [J]. Free Radic Biol Med, 2011, 50(10): 1355-1367

[27] Sato A, Hoshino Y, Hara T, et al. Thioredoxin-1 ameliorates cigarette smoke-induced lung inflammation and emphysema in mice [J]. J Pharmacol Exp Ther, 2008, 325(2): 380-388

[28] Nakamura T, Nakamura H, Hoshino T, et al. Redox regulation of lung inflammation by thioredoxin [J]. Antioxidants and Redox Signalling ,2005,7(1-2): 60-71

[29] Miwa K, Kishimoto C, Nakamura H, et al. Serum thioredoxin and alpha-tocopherol concentrations in patients with major risk factors [J]. Circulation Journal, 2005, 69(3): 291-294

[30] Ueno M, Masutani H, Arai RJ, et al. Thioredoxin-dependent redox regulation of p53-mediated p21 activation [J]. J Biol Chem, 1999,274 (50): 35809-35815

[31] Powis G, Montfort WR. Properties and biological activities of thioredoxins [J]. Annu Rev Pharmacol Toxicol, 2001, 41: 261-295

[32] Tiitto L, Kaarteenaho-Wiik R, Sormunen R, et al. Expression of the thioredoxin system in interstitial lung disease [J]. J Pathol, 2003, 201 (3): 363-370

[33] Zhang S, Xu N, Nie J, et al. Proteomic alteration in lung tissue of rats exposed to cigarette smoke [J]. Toxicol Lett, 2008,178(3): 191-196

[34] Rabe KF, Hurd S, Anzueto A, et al. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary [J]. Am J Respir Crit Care Med, 2007, 176 (6): 532-555

[35] Montuschi P, Macagno F, Parente P, et al. Effects of cyclo-oxygenase inhibition on exhaled eicosanoids in patients with COPD [J]. Thorax, 2005, 60(10): 827-833

[36] Harper R, Wu K, Chang MM, et al. Activation of nuclear factor-kappa b transcriptional activity in airway epithelial cells by thioredoxin but not by N-acetyl-cysteine and glutathione [J]. Am J Respir Cell Mol Biol, 2001, 25(2): 178-185

[37] Zhang S, Xu N, Nie J, et al. Proteomic alteration in lung tissue of rats exposed to cigarette smoke [J]. Toxicol Lett, 2008, 178(3): 191-196

[38] Hoshino Y, Nakamura T, Sato A, et al. Neurotropin demonstrates cytoprotective effects in lung cells through the induction of thioredoxin-1 [J]. Am J Respir Cell Mol Biol, 2007, 37(4):438-446

[39] Lehtonen ST, Ohlmeier S, Kaarteenaho-Wiik R, et al. Does the oxidative stress in chronic obstructive pulmonary disease cause thioredoxin/peroxiredoxin oxidation [J]. Antioxid Redox Signal, 2008,10 (4): 813-819

[40] Mercken EM, Hageman GJ, Langen RC, et al. Decreased exercise-induced expression of NF- {kappa}B regulated genes in muscle of COPD patients [J]. Chest, 2011, 139(2): 337-346