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不同麻醉方法对食管癌手术患者免疫及认知功能的影响

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摘要 目的:探讨全麻或全麻复合硬膜外麻醉对食管癌手术患者的 T 细胞水平及术后认知功能的影响。**方法:**选择 2014 年 1 月至 2015 年 12 月于我院择期行开胸手术的食管癌患者 100 例为研究对象,根据手术时间顺序分为观察组(全麻复合硬膜外麻醉)和对照组(全麻),每组 50 例,观察记录两组患者诱导前、插管时、术中 1 h、拔管后的平均动脉压(MAP)、血氧饱和度(SpO₂)和心率(HR);两组患者术前 30 min、术后 2 h、术后 2 d 和术后 7 d 的 T 细胞亚群水平,包括 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺;两组患者术前 1 d、术后 6 h、术后 1 d、术后 3 d 的认知功能;术后认知功能障碍(POCD)发生率。**结果:**诱导前观察组和对照组患者的 MAP、SpO₂ 和 HR 比较,差异均不显著(P>0.05),插管时、术中 1 h 和拔管后观察组患者的 MAP 和 HR 水平均明显低于对照组(P<0.05),而 SpO₂ 明显高于对照组(P<0.05)。术后 2 h,观察组和对照组的 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 值均较术前 30 min 明显降低(P<0.05),但两组间各指标值无显著性差异(P>0.05);术后 2 d,观察组的 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 值均明显高于对照组(P>0.05)。术后 7 d,两组的 T 细胞亚群水平均较术前 30 min 无显著性差异(P>0.05)。术后 6 h 和术后 1 d,两组的 MMSE 评分均较术前 1 d 明显下降(P<0.05),观察组术后 1 d、3 d 和 7 d 的 MMSE 评分均明显高于对照组(P<0.05)。术后 6 h,观察组的 POCD 发生率明显低于对照组(P<0.05),术后 1 d 和 3 d 观察组的 POCD 发生率低于对照组,但无统计学差异(P>0.05)。**结论:**与单凭全麻比较,全麻复合硬膜外麻醉对食管癌手术患者的 T 细胞水平及术后认知功能的影响较小,术后恢复快。

关键词:全麻复合硬膜外麻醉;食管癌;T 细胞水平;认知功能

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Effects of Different Anesthesia Methods on Immunity Function and Cognitive Dysfunction in Patients Undergoing Esophageal Cancer

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ABSTRACT Objective: To compare the effects of general anesthesia combined with epidural anesthesia and general anesthesia on t-cell immunity function and postoperative cognitive dysfunction in patients undergoing esophageal cancer. **Methods:** 100 cases of patients undergoing esophageal cancer in our hospital from January 2014 to December 2015 were divided into observation group (n=50, general anesthesia combined with epidural anesthesia) and control group (n=50, general anesthesia). The MAP, SpO₂, HR and the levels of CD3⁺, CD4⁺, CD8⁺ and CD4⁺/CD8⁺ in two groups were compared. **Results:** There was no significant differences in the mean arterial pressure(MAP), SpO₂ and heart rate(HR) before the induction between two groups(P>0.05); During intubation, intraoperative 1 h and after extubation, MAP and HR of patients in the observation group was significantly lower than that of the control group (P<0.05), and SpO₂ was significantly higher than that of the control group (P<0.05); after 2 hours of operation, the levels of CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ of two groups were significantly lower than that of 30 min of preoperation (P<0.05), but there was no significant differences between two groups (P>0.05); After 2 d of operation, the levels of CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ of the observation group was significantly higher than that of the control group (P<0.05); After 7 d of operation, the levels of CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ of two groups were back to normal. After 6 h and 1 d of operation, MMSE scores of two groups were significantly lower than that of 1 day of preoperation (P<0.05), MMSE scores of the observation group was significantly higher than that of the control group after 1,3,7 d of operation (P<0.05); after 6 h of operation, POCD incidence rate of the observation group was significantly lower than that of the control group(P<0.05). **Conclusions:** Compared with general anesthesia, general anesthesia combined with epidural anesthesia can effectively reduce the influence to t-cell immunity function and postoperative cognitive dysfunction in patients undergoing esophageal cancer.

Key words: General anesthesia combined with epidural anesthesia; Esophageal cancer; T-cell immunity function; Cognitive dysfunction

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前言

开胸手术是目前临床治疗食管癌的主要治疗手段,手术创伤较大^[1,2]。全麻或全麻复合硬膜外麻醉是目前临床外科手术应用较为广泛的麻醉方法。但研究显示,麻醉会对患者的免疫系统和认知功能带来一定的损伤^[3,4],近年来临床关于全麻或全麻复合硬膜外麻醉对于食管癌手术患者的免疫系统功能的影响研究较为多见^[5,6],但关于其对食管癌患者认知功能的影响研究较少见,因此本研究选择2014年1月至2015年12月于我院择期行开胸手术的食管癌患者100例为研究对象,在分析全麻或全麻复合硬膜外麻醉对于食管癌手术患者的免疫系统功能影响的同时,进一步探讨其对食管癌患者认知功能的影响,从而为临床更加全面的评价全麻或全麻复合硬膜外麻醉在食管癌手术中的效果,以及为手术中麻醉方法的选择提供参考。

1 资料与方法

1.1 一般资料

选择2014年1月至2015年12月于我院择期行开胸手术的食管癌患者100例为研究对象,所有患者均经临床症状、实验室、影像学检查及术后病理确诊;麻醉前依据美国麻醉医师协会制定的ASA分级标准对病人的体质状况和手术危险性进行分类,均为I和II级,术前简易精神状态量表(MMSE)评分大于24分。排除NYHA分级(纽约心功能分级)III级及以上患者,排除有严重肝肾功能不全、免疫和内分泌系统疾病的患者。本研究获得我院伦理委员会批准,所有患者均知情同意。

将100例患者根据手术时间顺序分为观察组和对照组,每组50例,观察组中男27例,女23例,年龄50-75岁,平均年龄(62.5±9.1)岁,体重50-78 kg,平均(60.3±8.8)kg,手术时间150-230 min,平均手术时间(190.6±32.7)min,术中出血量200-280 mL,平均术中出血量(250.5±35.5)mL,ASA I级28例,II级22例;对照组中男26例,女24例,年龄48-75岁,平均年龄(60.6±10.2)岁,体重50-80 kg,平均(60.9±9.3)kg,手术时间150-230 min,平均手术时间(195.5±35.3)min,术中出血量200-280 mL,平均术中出血量(251.5±36.6)mL,ASA I级27例,II级23例。两组患者的基线资料比较无统计学差异(P>0.05)。

1.2 麻醉方法

两组患者术前均禁食8 h,入室前30 min肌肉注射0.1 g的苯巴比妥和0.5 mg的阿托品。入室后开放静脉通道,监测患者动脉压(MAP)、血氧饱和度(SpO₂)、心率(HR)等生命体征。

观察组患者均于麻醉诱导前行T6-T7椎管间隙硬膜外腔穿刺置管,穿刺成功后试注入1%的利多卡因和5%的罗哌卡因混合液5 mL,观察5 min,待出现麻醉平面后继续注入5-8 mL混合液,使麻醉平面维持在T4-T5,之后进行麻醉诱导。对照组无穿刺过程,直接麻醉诱导。两组患者的麻醉诱导方案相同:咪唑安定0.05 mg/kg,丙泊酚1.5 g/mL,罗库溴铵0.9 mg/kg和芬太尼1.0 mg/kg,麻醉诱导成功后气管插管,机械通气。两组术中维持麻醉方法:对照组持续泵入丙泊酚2 g/mL,芬太尼3 mg/kg/h,根据麻醉深度(BIS)吸入0.5%-1.5%七氟烷,使麻醉深度BIS维持在40-50;观察组在对照组维持方法的基础之上每隔40-50 min经硬膜外导管追加5 mL混合液。

1.3 观察指标

(1)观察记录两组患者诱导前、插管时、术中1 h、拔管后的MAP、SpO₂和HR;(2)T细胞亚群水平:分别于术前30 min、术后2 h、术后2 d和术后7 d抽取患者肘静脉血5 mL,采用流式细胞仪(艾森生物(杭州)有限公司,型号:NovoCyte D1041)检测患者血中的T细胞亚群水平,包括CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺的数量;(3)两组患者术前1 d,术后6 h,术后1 d,术后3 d的认知功能及术后认知功能障碍(POCD)发生率。认知功能采用简易精神状态量表(MMSE)评定^[7],评定内容包括定向力、记忆力、注意力和计算力、回忆能力、语言能力,总分30分,分值越低表示认识功能障碍越严重,术后评分低于术前评分2分者,评定为POCD^[8]。

1.4 统计学分析

采用SPSS17.0对以上所得数据进行统计分析,计数资料以%表示,采用卡方检验,计量资料以均值±标准差表示,采用t检验,以P<0.05表示差异有统计学意义。

2 结果

2.1 两组不同时间点 MAP、SpO₂ 和 HR 比较

诱导前观察组和对照组患者的MAP、SpO₂和HR比较,差异均不显著(P>0.05),在插管时、术中1 h和拔管后观察组患者的MAP和HR水平均明显低于对照组(P<0.05),而SpO₂明显高于对照组(P<0.05)。与诱导前比较,观察组在插管时、术中1 h和拔管后的MAP明显降低,SpO₂明显升高(P<0.05),HR仅在拔管后明显高于诱导前(P<0.05),对照组在插管时、术中1 h和拔管后的SpO₂,HR均明显升高(P<0.05),而MAP在拔管后明显高于诱导前(P<0.05)。

表1 两组不同时间点 MAP、SpO₂ 和 HR 比较

Table 1 Comparison of the levels of MAP, SpO₂ and HR of two groups

Indexes	Groups	Before anesthesia induction	Tracheal intubation	Intra-operative 1 h	After pulling tubes
MAP(mmHg)	Observation group	100.45± 8.21	95.22± 6.69 [°]	93.11± 7.03 [°]	99.05± 7.05 [°]
	Control group	100.03± 8.55	98.85± 7.26	102.74± 5.56	103.32± 5.63 [°]
SpO ₂ (%)	Observation group	95.68± 2.05	97.36± 1.03 [°]	98.96± 0.68 [°]	99.22± 0.45 [°]
	Control group	95.45± 2.13	96.89± 1.19 [°]	97.12± 0.88 [°]	98.45± 0.86 [°]
HR(beats/min)	Observation group	86.82± 11.21	89.90± 12.53 [°]	90.66± 13.20 [°]	94.50± 12.01 [°]
	Control group	86.55± 11.16	94.01± 11.85 [°]	98.37± 14.50 [°]	105.29± 14.88 [°]

Note: Compared with control group, [°] P<0.05; Compared with the before anesthesia induction, [°] P<0.05.

2.2 两组 T 细胞亚群水平比较

术前 30 min 观察组和对照组的 $CD3^+$ 、 $CD4^+$ 、 $CD8^+$ 、 $CD4^+/CD8^+$ 值均无显著性差异 ($P>0.05$); 术后 2 h, 观察组和对照组的 $CD3^+$ 、 $CD4^+$ 、 $CD8^+$ 、 $CD4^+/CD8^+$ 值均较术前 30 min 明显降低 ($P<0.05$), 但两组间各指标值无显著性差异 ($P>0.05$); 术后 2 d, 两组的 $CD3^+$ 、 $CD4^+$ 值均明显低于术前 30 min ($P<0.05$), 观

察组的 $CD8^+$ 值明显高于术前 30 min ($P<0.05$), 对照组的 $CD8^+$ 值明显低于术前 30 min ($P<0.05$), 观察组和对照组的 $CD4^+/CD8^+$ 值均明显低于术前 30 min ($P<0.05$), 观察组的各指标均明显高于对照组 ($P<0.05$)。术后 7 d, 两组的 T 细胞亚群水平均较术前 30 min 无显著性差异 ($P<0.05$)。

表 2 两组 $CD3^+$ 、 $CD4^+$ 、 $CD8^+$ 、 $CD4^+/CD8^+$ 水平比较

Table 2 Comparison of the levels of $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ of two groups

Indexes	Groups	Preoperation 30 min	Postoperation 2 h	Postoperation 2 d	Postoperation 7 d
$CD3^+$	Observation group	62.33± 3.58	49.10± 5.93 [°]	58.80± 6.71 ^{° °}	62.06± 5.66
	Control group	62.51± 3.99	49.21± 5.80 [°]	52.02± 5.97 [°]	61.75± 4.83
$CD4^+$	Observation group	38.56± 6.23	25.09± 6.51 [°]	34.87± 7.02 ^{° °}	39.21± 8.80
	Control group	38.73± 6.55	25.10± 6.43 [°]	28.33± 6.69 [°]	38.66± 6.84
$CD8^+$	Observation group	27.02± 6.12	24.23± 5.65 [°]	28.80± 6.31 ^{° °}	28.98± 8.54
	Control group	27.10± 6.11	24.34± 5.60 [°]	25.51± 6.21 [°]	27.89± 6.37
$CD4^+/CD8^+$	observation group	1.43± 0.33	1.04± 0.25 [°]	1.21± 0.36 ^{° °}	1.35± 0.85
	control group	1.42± 0.35	1.04± 0.26 [°]	1.11± 0.28 [°]	1.38± 0.58

Note: Compared with preoperation 30 min, [°] $P<0.05$; Compared with control group, ^{° °} $P<0.05$.

2.3 两组不同时间点 MMSE 评分比较

术前 1 d, 观察组和对照组的 MMSE 评分比较无统计学差异 ($P>0.05$), 术后 6 h 和术后 1 d, 两组的 MMSE 评分均较术前 1 d 明显下降 ($P<0.05$); 术后 3 d, 观察组的 MMSE 评分与术前

比较无统计学差异 ($P>0.05$), 对照组的 MMSE 评分仍明显低于术前 1 d ($P<0.05$); 观察组术后 6 h、1 d、3 d 的 MMSE 评分均明显高于对照组 ($P<0.05$)。

表 3 两组不同时间点 MMSE 评分比较

Table 3 Comparison of MMSE scores of two groups

Groups	Cases	Preoperation 1 d	Postoperation 6 h	Postoperation 1 d	Postoperation 3 d
Observation group	50	28.05 1.13	24.57 1.06 ^{° °}	26.88 1.10 ^{° °}	27.94 0.95 [°]
Control group	50	27.30 1.91	20.02 2.01 [°]	25.82 2.16 [°]	26.30 2.64 [°]

Note: Compared with preoperation 1 d, [°] $P<0.05$; Compared with control group, ^{° °} $P<0.05$.

2.4 两组术后 POCD 发生情况比较

术后 6 h, 观察组的 POCD 发生率明显低于对照组 ($P<0.05$), 术后 1 d 和 3 d 观察组的 POCD 发生率低于对照组, 但无

统计学差异 ($P>0.05$)。

表 4 两组术后 POCD 发生情况比较[n(%)]

Table 4 Comparison of POCD incidence of two groups

Groups	Cases	Postoperation 6 h	Postoperation 1 d	Postoperation 3 d
Observation group	50	8 (16.00) [°]	3 (6.00)	0 (0.00)
Control group	50	16 (32.00)	4 (8.00)	2 (0.04)

Note: Compared with control group, [°] $P<0.05$.

3 讨论

开胸手术虽然是目前治疗食管癌的首选治疗方法, 但手术创伤大, 术中均需麻醉, 麻醉、手术创伤等因素均会对患者的免疫功能和认知功能带来损害, 尤其是老年患者, 影响患者的术后恢复^[9,10]。全麻或全麻复合硬膜外麻醉是目前临床外科手术应用较为广泛的麻醉方法, 且安全性和麻醉效果均已得到临床证实^[11,12]。研究显示, 与单凭全麻比较, 全麻复合硬膜外麻醉对手术患者的循环系统指标影响较小^[13], 本研究结果同样显示, 在插管时、术中 1 h 和拔管后观察组患者的 MAP 和 HR 水平均明显低于对照组 ($P<0.05$), 而 SpO_2 明显高于对照组 ($P<0.05$)。

与诱导前比较, 观察组在插管时、术中 1 h 和拔管后的 MAP 明显降低, SpO_2 明显升高 ($P<0.05$), HR 仅在拔管后明显高于诱导前 ($P<0.05$), 对照组在插管时、术中 1 h 和拔管后的 SpO_2 、HR 均明显升高 ($P<0.05$), 而 MAP 在拔管后明显高于诱导前 ($P<0.05$)。说明手术刺激引起了机体的应激反应, 从而使患者的 MAP、 SpO_2 和 HR 发生变化, 但观察组的 MAP、 SpO_2 和 HR 变化优于对照组, 可能原因为单凭全麻不能完全阻断手术对脑垂体和肾上腺的刺激, 而导致患者呼吸循环紊乱, 而全麻复合硬膜外麻醉可阻滞节前交感神经的兴奋, 从而有效抑制手术引起的应激反应, 减慢心率、降低血压、升高血氧饱和度等^[14]。

T 淋巴细胞是机体细胞免疫的主群,在机体免疫应答和免疫调节中发挥重大作用,CD3⁺T 细胞代表细胞免疫的整体水平,按细胞表面分化抗原(CD)的不同,可分为 CD4⁺ 和 CD8⁺, CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 水平的相对降低均提示患者细胞免疫功能降低^[15,16]。目前,临床对于麻醉引起的免疫功能抑制大多通过 T 细胞亚群的测定来判断。本研究中,术前 30 min,观察组和对照组的 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 值均无显著性差异($P>0.05$);术后 2 h,观察组和对照组的 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 值均较术前 30 min 明显降低($P<0.05$),但两组间各指标值无显著性差异($P>0.05$);可能原因为手术创伤、麻醉引起机体神经内分泌系统紊乱,使 T 细胞的免疫调节网络失衡,而引起机体一定程度的免疫抑制,使 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 值下降。术后 2 d,两组的 CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺ 水平开始逐渐恢复,观察组的各指标均明显高于对照组($P<0.05$)。术后 7 d,两组的 T 细胞亚群水平均较术前 30 min 无显著性差异($P>0.05$)。说明与单凭静脉麻醉相比,全麻复合硬膜外麻醉可明显改善手术创伤引起的免疫抑制,可能原因为全麻复合硬膜外麻醉的麻醉效果较好,可减轻患者的应激反应。本研究结果与董桂祥等研究结果一致^[17]。

本研究还显示,术后 6 h 和术后 1 d,两组的 MMSE 评分均较术前 1 d 明显下降($P<0.05$);说明手术及麻醉可引起食管癌患者认知功能障碍,可能原因为手术的强烈持续刺激抑制中枢胆碱能系统,引起患者大脑海马区损害而影响学习和记忆能力^[18]。术后 3 d,观察组的 MMSE 评分与术前比较无统计学差异($P>0.05$),对照组的 MMSE 评分仍明显低于术前 1 d($P<0.05$);观察组术后 1 d、3 d 和 7 d 的 MMSE 评分均明显高于对照组($P<0.05$),术后 6 h,观察组的 POCD 发生率明显低于对照组($P<0.05$)。说明观察组术后认知功能的恢复速度较对照组快,考虑可能与全麻复合硬膜外麻醉使患者的术中应激反应较轻,对认知功能的损害较轻以及术后体内残余麻醉药对中枢神经系统的影响有关^[19,20]。

综上所述,与单凭全麻比较,全麻复合硬膜外麻醉对食管癌手术患者的 T 细胞水平及术后认知功能的影响较小,术后恢复快。

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