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贮存式自体成分输血对胃肠肿瘤根治术患者 T 淋巴细胞亚群、血液流变学和预后的影响 *

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摘要 目的:研究贮存式自体成分输血对胃肠肿瘤根治术患者 T 淋巴细胞亚群、血液流变学以及预后的影响。**方法:**选取 2016 年 12 月~2017 年 12 月我院收治的 95 例行胃肠肿瘤根治术的胃肠肿瘤早期患者作为研究对象。按随机数表法分为 A 组(n=47, 贮存式自体成分输血)和 B 组(n=48, 异体成分输血)。比较两组患者血常规指标[红细胞计数(RBC)、血红蛋白(Hb)、血细胞比容(Hct)]、免疫功能指标(CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺)、血液流变学指标[红细胞沉降率、平均血液黏度、红细胞刚性指数及红细胞变形指数]的变化。随访患者 2 年,采用 Kaplan-Meier 曲线分析两组预后情况。**结果:**术前至术后 7 d 时间段 A 组的 CD3⁺、CD4⁺ 水平及 CD4⁺/CD8⁺ 呈先降低后升高趋势,且术后 7 d 已恢复至术前水平;B 组术后 1 d、3 d、7 d 的 CD3⁺、CD4⁺ 水平及 CD4⁺/CD8⁺ 明显低于 A 组($P<0.05$),两组 CD8⁺ 水平相比无差异($P>0.05$)。两组术后 7 d 的 RBC、Hct、Hb 分别较输血前下降($P<0.05$),但两组间比较差异无统计学意义($P>0.05$);两组患者术后 7 d 的红细胞沉降率均升高,但 A 组低于 B 组($P<0.05$),两组患者术后的红细胞变形指数、平均血液黏度和红细胞刚性指数比较无差异($P>0.05$)。Kaplan-Meier 检验结果显示,A 组较 B 组生存率明显升高($P<0.05$)。**结论:**贮存式自体成分输血对胃肠肿瘤根治术患者红细胞沉降率、细胞免疫功能的影响程度较异体成分输血减轻,且贮存式自体成分输血可以明显提高患者的术后生存率。

关键词: 胃肠肿瘤根治术;自体输血;异体输血;T 细胞亚群;血液流变学;预后

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The Effect of Stored Autologous Blood Transfusion on T Lymphocyte Subsets, Hemorheology and Prognosis in Patients with Radical Resection of Gastrointestinal Tumor*

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ABSTRACT Objective: To study effect of stored autologous blood transfusion on T lymphocyte subsets, hemorheology and prognosis in patients with radical resection of gastrointestinal tumor. **Methods:** From December 2016 to December 2017, 95 patients with early gastrointestinal tumor undergoing radical gastrectomy in our hospital were selected as the study object. According to the method of random number table, the patients were divided into two groups: Group A (n=47, stored autologous component transfusion) and Group B (n=48, allogeneic component blood transfusion group). The routine blood index [red blood cell count (RBC), hemoglobin (Hb), hematocrit(Hct)], immune function index (CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺), hemorheology index [erythrocyte sedimentation rate, average blood viscosity, erythrocyte rigidity index and erythrocyte deformation index] change of two groups patients were compared. Patients were followed up for 2 years, and the prognosis of the two groups was analyzed by Kaplan-Meier curve. **Results:** The levels of CD3⁺, CD4⁺, CD4⁺/CD8⁺ in group A decreased first and then increased, and returned to the preoperative level 7 d after operation. The levels of CD3⁺, CD4⁺, CD4⁺/CD8⁺ in group B were significantly lower than those in group A 1 d, 3 d, 7 d after operation($P<0.05$), but there was no difference in the level of CD8⁺ between the two groups($P>0.05$). The RBC, Hct and Hb of the two groups decreased at 7 d after operation compared with that before transfusion ($P<0.05$), but there was no statistically significant difference between the two groups ($P>0.05$). The erythrocyte sedimentation rate of both groups was increased 7 d after operation, but the Group A was lower than Group B ($P<0.05$). There were no statistically significant differences in erythrocyte deformation index, mean blood viscosity and erythrocyte rigidity index between the two groups ($P>0.05$). Kaplan-Meier test results showed that the survival rate of the Group A was significantly higher than that of the

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Group A ($P<0.05$). **Conclusion:** The effect of stored autologous component transfusion on erythrocyte sedimentation rate and cellular immune function in patients undergoing radical resection of gastrointestinal tumor are less than those of allogeneic component blood transfusion, and the survival rate of the patients was significantly improved by stored autologous component transfusion.

Key words: Radical resection of gastrointestinal tumor; Autologous blood transfusion; Allogeneic blood transfusion; T cell subsets; Hemorheology; Prognosis

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前言

胃肠肿瘤是指胃肠道的恶性肿瘤,患者常表现为腹部包块、全身症状、血便和肠梗阻等症状^[1,2]。目前,采用根治性手术切除是其常用治疗方法,但在手术期间,胃肠肿瘤患者往往常因营养不良、出血等多种因素导致贫血而必须输血^[3,4]。贮存式自体输血是在术前根据患者情况,在术前1周预先抽取并储存其自身全血,并在需要输血治疗时,将自体血(术前采集)输入病人体内,满足患者本人手术或急救治疗需求的一种血液保护技术^[5,6]。血液贮存过程中,白细胞裂解释放可溶性抗原,患者回输长时间贮存悬浮红细胞,容量治疗效果降低,但可能会导致免疫抑制。输血量越大,患者体内的异源白细胞就越多,理论上对免疫功能影响更重。血液流变学与组织器官的微循环灌注有关,而红细胞的流变学特性是影响血液流变学的重要因素,其中红细胞的聚集指数和刚性指数能反映相关特性^[7,8]。本研究拟比较贮存式自体成分输血与异体成分输血对胃肠肿瘤根治术患者细胞免疫功能、血液流变学和预后的影响,为胃肠肿瘤根治术患者输血方案的选择提供依据。

1 资料与方法

1.1 一般资料

选取2016年12月~2017年12月我院收治的行胃肠肿瘤根治术的胃肠肿瘤早期患者95例。纳入标准:(1)拟行切除根治术,ASA分级^①为I或II级;(2)无内分泌或免疫性疾病,无放疗、化疗及激素治疗史者;(3)心肝脾肺肾等脏器及凝血功能检查未见异常者;(4)治疗期间未使用影响免疫功能药物者;(5)术前血红蛋白(Hemoglobin, Hb) >110 g/L,血细胞比容(Hematocrit, Hct) >0.33 ;(6)术中患者平均失血量达到800毫升;(7)所有进行胃肠肿瘤根治术者均进行了MDT严格评估。排除标准:(1)合并严重肝肾功能不全者;(2)合并糖尿病、高血压等疾病者;(3)有严重感染或输血病史者;(4)合并心脏功能障碍、动脉粥样硬化者。按随机数表法分为A组($n=47$)和B组($n=48$)。其中A组男30例,女17例,年龄35~60岁,平均(43.49 ± 4.56)岁;体质指数 $19.2 \sim 23.8$ kg/m²,平均(21.52 ± 1.02)kg/m²,ASA分级:I级20例,II级27例;B组男32例,女16例,年龄36~63岁,平均(44.20 ± 5.13)岁;体质指数 $19.3 \sim 23.9$ kg/m²,平均(22.01 ± 1.13)kg/m²,ASA分级:I级22例,II级26例;两组一般资料比较无差异($P>0.05$),临床基线资料均衡可比。

1.2 方法

A组采用贮存式自体成分输血:术前1周采集患者自体血液400~600 mL,分离红细胞并贮存,其余成分回输患者体内,

术中常规输液,术中将贮存的红细胞回输于患者体内。B组采用异体成分输血:根据术中出血量、Hb、Hct和血流动力学情况酌情输注同等剂量异体红细胞悬液。

1.3 观察指标

(1)免疫功能指标检测:分别于手术前、输血前、术后1 d、术后3 d、术后7 d抽取患者静脉血6 mL,采用流式细胞仪(贝克曼库尔特商贸(中国)有限公司)进行T细胞亚群检测,包括CD3⁺、CD4⁺、CD8⁺水平,计算CD4⁺/CD8⁺比值;(2)血常规指标及血液流变学指标检测:于输血前及术后7 d分别抽取静脉血2 mL,抗凝处理后采用MEN-C100A(40孔)全自动血液流变动态分析仪(上海泰益医疗仪器设备)在37℃条件下测定患者Hb、Hct、红细胞计数(RBC)、红细胞沉降率、平均血液黏度、红细胞刚性指数及红细胞变形指数的变化。所有操作严格按照试剂盒(江苏晶美生物科技有限公司)说明进行。(3)术后2年进行电话、短信随访和复查方式,统计2年内各组患者生存率。

1.4 统计学方法

采用SPSS24.0软件分析数据。符合正态分布的计量资料以($\bar{x} \pm s$)表示,组间比较行t检验;计数资料以率表示,行 χ^2 检验,采用Kaplan-Meier法分析两组的预后情况。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组T淋巴细胞比较

术前及输血前两组患者外周血中CD3⁺、CD4⁺、CD8⁺、CD4⁺/CD8⁺比较均无统计学差异($P>0.05$),术后1 d两组CD3⁺、CD4⁺水平及CD4⁺/CD8⁺均开始下降,术前至术后7 d时间段A组的CD3⁺、CD4⁺水平及CD4⁺/CD8⁺呈先降低后升高趋势,且术后7 d已恢复至术前水平;B组CD3⁺、CD4⁺水平及CD4⁺/CD8⁺术前至术后1 d呈下降趋势,且术后3 d、7 d仍未回升。B组术后1 d、3 d、7 d的CD3⁺、CD4⁺水平及CD4⁺/CD8⁺明显低于A组($P<0.05$),两组CD8⁺水平相比无差异($P>0.05$)。见表1。

2.2 两组患者血常规指标比较

两组输血前RBC、Hct、Hb比较差异无统计学意义($P>0.05$)。两组术后7 d血常规指标RBC、Hct、Hb分别较输血前显著下降($P<0.05$),但组间比较无差异($P>0.05$),见表2。

2.3 两组患者血液流变学指标比较

输血前两组患者血液流变学指标比较差异无统计学意义($P>0.05$)。术后7 d,两组患者红细胞沉降率升高,但A组低于B组($P<0.05$),两组平均血液黏度、红细胞刚性指数、红细胞变形指数在输血前、术后7 d组间比较差异无统计学意义($P>0.05$),见表3。

表 1 两组 T 淋巴细胞比较($\bar{x} \pm s$)Table 1 Comparison of T lymphocytes between the two groups ($\bar{x} \pm s$)

Groups	Time	CD3 ⁺ (%)	CD4 ⁺ (%)	CD8 ⁺ (%)	CD4 ⁺ /CD8 ⁺
Group A(n=47)	Before operation	74.83± 7.43	38.42± 4.67	31.12± 5.21	1.23± 0.11
	Before blood transfusion	70.71± 8.22	36.44± 6.79	31.09± 5.68	1.17± 0.07
	1 d after operation	66.36± 7.55	33.74± 6.23	31.08± 5.53	1.09± 0.11
	3 d after operation	68.11± 7.46	33.11± 5.85	31.32± 4.38	1.06± 0.06
	7 d after operation	72.58± 9.76	36.37± 5.88	31.28± 4.63	1.16± 0.12
Group B(n=48)	Before operation	74.89± 6.77	39.14± 5.45	32.05± 5.82	1.22± 0.09
	Before blood transfusion	70.35± 8.68	36.57± 6.26	31.85± 6.61	1.15± 0.11
	1 d after operation	60.17± 6.57*	28.85± 5.79*	30.35± 5.80	0.95± 0.08*
	3 d after operation	59.35± 7.03*	27.67± 5.83*	30.26± 4.77	0.91± 0.08*
	7 d after operation	58.58± 7.83*	26.75± 6.52*	32.75± 4.18	0.82± 0.05*

Note: compared with group A, * $P<0.05$.表 2 两组患者血常规指标比较($\bar{x} \pm s$)Table 2 Comparison of blood routine indicators between the two groups ($\bar{x} \pm s$)

Groups	RBC($10^{12}/L$)		Hb(g/L)		Hct	
	Before blood transfusion	7 d after operation	Before blood transfusion	7 d after operation	Before blood transfusion	7 d after operation
Group A(n=47)	4.21± 0.49	3.46± 0.44 [#]	121.01± 16.86	66.13± 13.56 [#]	0.62± 0.07	0.49± 0.11 [#]
Group B(n=48)	4.34± 0.46	3.59± 0.51 [#]	115.92± 16.53	65.17± 14.22 [#]	0.60± 0.09	0.47± 0.08 [#]
t	1.326	1.323	0.317	1.478	1.203	1.008
P	0.188	0.189	0.755	0.143	0.232	0.316

Note: compared with before blood transfusion, [#] $P<0.05$.表 3 两组患者血液流变学指标比较($\bar{x} \pm s$)Table 3 Comparison of hemorheology indexes between the two groups ($\bar{x} \pm s$)

Groups	Erythrocyte sedimentation rate (mm/h)		Mean blood viscosity(m Pa/s)		Erythrocyte rigidity index		Erythrocyte deformation index	
	Before blood transfusion	7 d after operation	Before blood transfusion	7 d after operation	Before blood transfusion	7 d after operation	Before blood transfusion	7 d after operation
Group A (n=47)	33.44± 32.53	40.23± 29.17 [#]	4.92± 1.58	4.58± 1.48	5.68± 0.73	5.63± 0.85	0.61± 0.18	0.67± 0.25
Group B (n=48)	33.67± 29.61	51.92± 23.29 [#]	4.74± 0.81	4.61± 1.73	5.71± 0.87	5.79± 0.71	0.64± 0.21	0.69± 0.23
t	0.036	2.147	0.701	0.091	0.186	0.997	0.747	0.203
P	0.971	0.034	0.485	0.928	0.856	0.322	0.457	0.840

Note: compared with before blood transfusion, [#] $P<0.05$.

2.4 两组患者预后情况比较

随访 2 年,用 Kaplan-Meier 检验结果显示,2 年内,A 组较 B 组生存率明显升高,Kaplan Meier 结果显示,A 组术后 2 年总生存率为 63.83%(30/47),B 组术后 2 年总生存率为 52.08%(25/48),两组比较差异有统计学意义(Log Rank $\chi^2=5.334$, $P=0.047$),见图 1。

3 讨论

胃肠肿瘤根治术需要完整切除病灶处,并清扫附近淋巴结,因胃肠被切除后,影响食物在体内的消化吸收,导致内因子缺乏、营养不良,降低免疫力,并造成贫血,因此常常需要输血^[10,11]。异体输血可降低肿瘤患者免疫功能及产生与输血相关肺损伤;另外,异体输血可增加患者败血症发生率、感染率,延长住院时间,甚至增加患者死亡率^[12,13]。自体输血是一种输血治疗方法,是采用患者自身的全血或成分血,满足本人手术或大失血后回输^[14]。自体输血有着异体输血无法比拟的优点^[15]。首

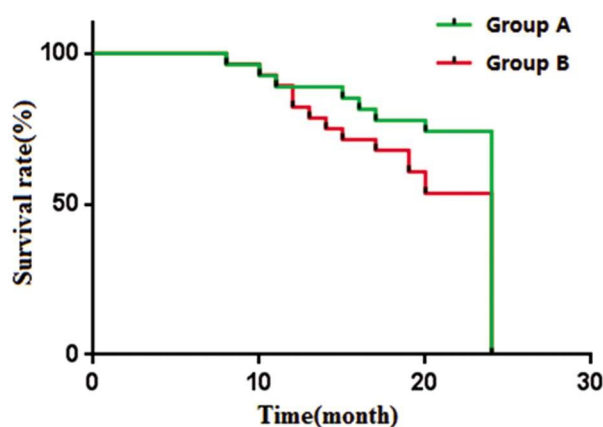


图1 两组患者2年的生存曲线

Fig.1 The 2-year survival curves of the two groups

先,自体输血较异体输血更加安全,可以避免经血液传播的疾病,如梅毒、艾滋病、肝炎病毒等。自体输血还可以避免异体输血产生的同种免疫反应,如溶血性发热反应、荨麻疹反应、过敏反应等。贮存式自体输血对机体各方面包括免疫功能、凝血功能、生化指标等影响与异体输血相比更小^[16-18]。自体输血的费用较异体输血低,贮存式自体输血只收取一次性采血费(包括血袋费)、复查血型和血液存储的费用,是输注异体血费用的1/3,甚至更少。术前采集血液可刺激红细胞再生,提前动员造血功能,有效提升血红蛋白能力,而且贮存式自体输血可降低择期手术患者的平均住院日和术后感染率^[19]。

本研究结果显示,术后1 d、3 d、7 d, A组的CD3⁺、CD4⁺水平及CD4⁺/CD8⁺高于B组,这和周循等研究一致^[20],说明异体血的输入导致受血患者T淋巴细胞及其亚群改变,细胞免疫功能受到明显抑制。患者外周血中T淋巴细胞各亚群的数量或功能发生异常,导致机体免疫紊乱,其机制可能为异体全血中的白细胞碎片和血浆如人白细胞抗原,造成异体输血患者术后细胞免疫异常,导致免疫功能抑制^[21,22]。A组患者CD3⁺、CD4⁺水平及CD4⁺/CD8⁺术后7 d基本恢复正常,其原因可能是:①自体输血不含异体血中的免疫中性效应物质,减少了对自身免疫细胞的影响,降低了自身排斥反应,不会造成自身免疫应激反应,对免疫功能影响较小;②自体输血可正向调节细胞免疫,迅速恢复各细胞免疫指标;③与麻醉应激、手术有关,随着应激反应的减轻,逐渐恢复各细胞亚群数量。机体免疫反应以细胞免疫为主,故T淋巴细胞在抗肿瘤生长、细胞免疫中具有重要作用^[23,24]。

本研究结果显示A组的患者的平均血液黏度、红细胞刚性指数、红细胞变形指数在术后没有显著的变化,这是血液通过过滤、离心、洗涤后,大部分游离血红蛋白、裂解后的红细胞碎片以及炎性介质被清除,因此输入的红细胞大多为正常红细胞,对红细胞的聚集、变形功能无明显影响。红细胞沉降率是指血液在静止状态下红细胞在自身血浆中的沉降速度^[25],本研究中术后红细胞沉降率均升高,但A组的升高幅度较B组更小,这可能与免疫排斥的清除作用有关,而自体输血引起的排斥反应较为轻微,故而红细胞性沉降率波动较小^[26,27]。本研究显示随访两年,A组术后2年总生存率高于B组,说明自体成分输血可在一定程度上改善患者生存预后,这是因为异体输血可

加重免疫抑制,导致患者机体的免疫失衡,进而影响预后^[28,29],且部分患者术后体内存在残留病灶,而残留病灶可出现生长、恶化及转移,致使患者术后出现复发,异体输血所介导的免疫抑制情况可影响清除残留病灶的效果,不利于患者术后恢复^[30]。

综上所述,胃肠肿瘤根治术患者采用贮存式自体成分输血可减少对其免疫功能的损害,还可减少手术中和手术后对异体血的需求,提高患者术后生存率。值得注意的是,由于肿瘤患者自体输血存在一定的血转移风险,因此进行输血方案的选择时必须经过严格的MDT评估,以避免血转移风险。

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