doi: 10.13241/j.cnki.pmb.2018.16.037

血液病患者单采血小板输注疗效的影响因素分析

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摘要 目的:探讨影响血液病患者血小板输注疗效的因素,为提高血液病患者的临床疗效提供参考依据。**方法:**选择 2013 年 1 月至 2015 年 12 月海南省人民医院收治的 156 例输注单采血小板的血液病患者为研究对象,所有患者单次输入血小板 12U (血小板数≥ 2.5× 10^{11} 个),观察输注后血小板计数纠正增加指数(CCI),分析病种、脾大、发热、年龄、性别对血小板输注疗效的影响。**结果:**血小板输注总有效率为 71.0%。再生障碍性贫血(AA)者血小板输注有效率为 65.9%、特发性血小板减少性紫癜(ITP)为 65.7%,急性白血病(AL)为 77.7%,骨髓增生异常综合征(MDS)为 71.9%,不同病种之间血小板输注有效率比较差异无统计学意义(*P>0.05*)。发热感染者血小板输注有效率为 69.9%,明显低于无发热感染者 (77.6%,*P<0.05*);脾不大者有效率为 74.9%,明显高于脾大者(52.86%,*P<0.05*);男性、女性有效率分别为 76.5%、75.8%,<60 周岁者与≧60 周岁者有效率分别为 72.0%、77.3%,差异均无统计学意义(*P>0.05*)。随着血小板输注次数的升高,血小板输注无效的发生率也显著升高。**结论:**发热及脾大是影响血液病患者血小板输注疗效的不利因素。

关键词:血液病;单采血小板;输注;疗效

中图分类号:R55; R457 **文献标识码:**A **文章编号:**1673-6273(2018)16-3167-03

Analysis of the Influencing Factors for the Clinical Efficacy of Platelet Transfusion in the Treatment of Patients with Hemopathy

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ABSTRACT Objective: To investigate the influencing factors for the clinical efficacy of platelet transfusion in the treatment of patients with hemopathy. **Methods:** 156 cases of patients with hemopathy who were treated by platelet transfusion in our hospital from January 2013 to December 2015 were selected. All the patients were given 12 U platelet (≥ 2.5× 10^{11}), the corrected count increment (CCI) after transfusion and the effect of disease category, splenomegalia, fever, age, gender with on the clinical efficacy of platelet transfusion were analyzed. **Results:** The total effective rate of platelet transfusion was 71.0%, which was 65.9%, 65.7%, 77.7% and 71.9% in patients with aplastic anemia(AA), idiopathic thrombocytopenic purpura(ITP), acute leukemia(AL), myelodysplastic syndrome (MDS) respecctively, no significant difference was found between different disease categories (*P>0.05*). The effective rate was 69.9% in febrile patients, which was obviously lower than those non-febrile patients (77.6%, *P<0.05*); the effective rate was 74.9%, which was overtly lower than those with splenomegalia(52.86%, *P<0.05*); no significant difference was found in the effective rate between male and female, <60 years old and years old (76.5% vs. 75.8%, 72.0% vs. 77.3%)(*P>0.05*). With the incease of transfusion times, the incidence of platelet transfusion refractoriness was gradually elevated (*P<0.05*). **Conclusions:** Splenomegalia and fever were adverse factors for the clinical efficacy of platelet transfusion in the treatment of patients with hemopathy.

Key words: Hemopathy; Apheresis platelets; Transfusion; Clinical efficacy

Chinese Library Classification(CLC): R55; R457 Document code: A

Article ID: 1673-6273(2018)16-3167-03

引言

血液病患者在疾病进展或骨髓抑制期常由于血小板减少或血小板功能缺陷引起出血,严重者可危及患者生命[1,2]。血小板输注已成为血液病患者一种有效的治疗方法,单采血小板输注已在临床普及应用。但临床数据表明部分患者在输注血小板后,血小板计数增加值未见明显升高甚至出现下降,明显低于临床预期,部分患者连续两次接受足够剂量的血小板输注后,仍处于无反应状态,出现血小板输注无效 (platelet transfusion refractoriness,PTR)[3-5]。研究表明影响血小板输注疗效的因素复杂多样,与患者自身基础疾病及单采血小板的性质均有相关性[6-8]。为提高血液病患者血小板输注的临床疗效,本研究选择了海南省人民医院 2013 年 1 月至 2015 年 12 月收治的 156 例采用输注机采血小板治疗的血液病患者的临床资料进行回顾性分析,结果报道如下。

1 资料与方法

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(收稿日期:2018-02-13 接受日期:2018-03-08)

1.1 临床资料

选择海南省人民医院 2013 年 1 月至 2015 年 12 月收治的 156 例采用输注机采血小板治疗的血液病患者，包括男性 89 例，女性 67 例，年龄 17～81 岁。患者均经临床及实验室检查确诊，包括再生障碍性贫血(AA)35 例，特发性血小板减少性紫癜(ITP)23 例，急性白血病(AL)43 例，骨髓增生异常综合征(MDS) 55 例。

1.2 血小板输注方案

所有单采血小板均由海南省血液中心提供，每个治疗量的单采血小板为 250-300 ML，血小板计数＞2.5× 10^{11} 个 / 袋。血小板输注指征：患者有皮肤及黏膜出血，伴或不伴内脏及颅内出血，血小板计数 <20× 10^{9}/L；血小板计数 <10× 10^{9}/L，临床无输血倾向 [3]。选择 ABO 和 Rh 血型同型的机采血小板进行输注。每位患者输注血小板 1～12 次。

1.3 血小板输注疗效评价

分别采集患者输注血小板前及输注后 24h 的静脉血进行血小板计数。观察患者出血情况有无改善及输注后血小板计数纠正增加指数(corrected count increment，CCI)。输注血小板后 24 h 的 CCI<4.5 为血小板输注无效。CCI= 输血后血小板增加数(× 10^{9}/L)× 体表面积(m^2)/ 输注血小板总数(× 10^{11})。记录患者有无发热、感染、脾大的情况。

1.4 统计学分析

采用 SPSS18.0 统计软件进行数据分析。计数资料以百分率表示，组间比较采用 x^2 检验，以 *P<0.05* 为差异有统计学意义。

2 结果

2.1 四种血液病患者治疗有效率的比较

156 例血液病患者中，血小板输注有效病例为 110 例，有效率为 71.0%，见表 1。其中，AL 患者血小板输注有效率为 77.7%；MDS 患者有效率为 71.9% ；AA 患者有效率为 65.9% ；ITP 患者有效率为 65.7%。四种血液病血小板输注有效率比较差异无统计学意义(*P*=0.337)。

表 1 四种血液病患者血小板输注有效率比较

Table 1 Comparison of the clinical efficacy of platelet transfusion between patients with AA, AL, MDS and ITP

Disease category	Case	Transfusion cases	Effective Cases	Effectively rate(%)
AA	35	85	56	65.9
AL	43	103	80	77.7
MDS	55	146	105	71.9
ITP	23	70	46	65.7
Total	156	404	287	71.0

2.2 影响血小板输注有效率的临床因素

血小板输注患者中，发热感染 239 例次，无发热感染 165 例次；脾大 89 例次，脾不大 315 例次。发热感染者血小板输注有效率 69.9%，明显低于无发热感染者(77.6%，*P<0.05*)。脾不大者血小板输注有效率为 74.9%，明显高于脾大者 (52.8%，*P<0.05*)。男性患者血小板输注有效率 76.5%，与女性患者血小板输注有效率相比差异无统计学意义(75.8%，*P>0.05*)。<60 周岁患者血小板输注有效率为 77.3%，与 >60 周岁患者相比差异无统计学意义(72.0%，*P>0.05*)。

表 2 不同临床特征患者血小板输注的有效率比较

Table 2 Comparison of the effective rate of platelet transfusion between patients with different clinical charateritics

Groups	Transfusion cases	Effective Cases(%)	*p*
Fever			
No	165	128(77.6)	
Yes	239	167(69.9)	0.032
Splenomegalia			
No	315	236(74.9)	
Yes	89	47(52.8)	0.014
Years old			
>60	193	139(72.0)	
<60	211	163(77.3)	0.437
Gender			
Male	230	176(76.5)	
Female	174	132(75.8)	0.794

2.3 血小板输注次数与 PTR 发生率的相关性

如表 3 所示，随着血小板输注次数的增加，患者 PTR 的发生率逐渐升高。血小板输注 1、2～8、≥ 8 次时，PTR 的发生率比较差异均有统计学意义（*P<0.05*）。

表 3 血小板输注次数与 PTR 发生率的关系

Table 3 Correlation of the platelet transfusion with the incidence of PTR

Transfusion times	Transfusion cases	Effective Cases(%)	Incidence of PTR[n(%)]
1	78	78	11(14.10)
2-8	46	204	52(25.49)
>8	32	122	62(50.81)
Total	156	404	125(30.94)

3 讨论

血小板输注治疗是临床上预防和缓解各种原因所致血小板减少或功能障碍进而引起出血的主要方法，其疗效不仅与供体血小板的质量有关，而且与患者同种自身免疫因素、发热、感染、弥散性血管内凝血(DIC)、出血、脾大等病理因素密切有关[9-11]。临床上主要采用 CCI 和血小板恢复百分率(PPR)以及患者出血状况有无改善评价血小板输注的临床效果[12]。由于血小板输注后患者出血状况改善程度不易量化，故本研究以 CCI≥ 4.5 作为血小板输注治疗有效的依据。

本研究中，156 接受血小板输注的总有效率为 71.0%，而再生障碍性贫血、特发性血小板减少性紫癜、急性白血病、骨髓增生异常综合征患者血小板输注有效率相当，并无统计学差异，但其中以特发性血小板减少性紫癜患者的有效输注率最低，这可能与患者自身产生抗血小板抗体加速了血小板的破坏有关。患者感染发热时，血小板隐蔽抗原暴露，可吸附 IgG 抗体，随后通过网状内皮系统清除这些被抗体包被的血小板，进而导致血小板生存期缩短[13]。本研究结果也显示有发热症状的血液病患者血小板输注有效率明显低于无发热感染的患者，也证实了这一点。脾大是致血小板输注无效的主要因素之一[14]。机体约 1/3 的血小板存在于脾池中，可以与循环池交换。在与血小板相关的疾病中，脾脏常是破坏血小板的部位，任何原因引起的脾大都可导致在脾脏被破坏的血小板比正常多 30%[15]。此外，由于脾脏的滤泡为 B 细胞区，与抗体生成有关，而生发中心是 B 淋巴细胞增生转化的场所，具有较强产生抗体的能力，因此生发中心数目及大小均可影响机体对抗原刺激的反应程度。本研究结果显示脾大患者较脾正常患者血小板输注有效率明显降低，也表明脾大是影响血小板输注临床效果不利因素。有效的血小板输注可减少血液病患者因血小板减少或功能障碍所致的出血。但多次进行血小板输注可能导致临床效果下降，甚至出现 PTR。在本研究中，输注次数 >8 次者 PTR 发生率高达 50.84%，且随着输注次数的增加，PTR 的发生率逐渐升高，表明输注血小板次数与 PTR 发生率具有明显的相关性。

为了提高血小板输注的有效性，需要去除可能导致血小板输注无效的不利因素，例如对存在 HLA 抗体和血小板特异性抗体的患者，应进行 HLA 配型或血小板交叉配型。另外，由于白细胞的存在以及血小板在保存中自行损伤与活化而释放的白细胞介素(IL)-1、IL-6、IL-8、肿瘤坏死因子、转化生长因子 B、血小板第 4 因子、牛甲状腺球蛋白等细胞因子均可能引起血小板输注无效，故临床上应当尽可能输注 24 h 内新鲜单采血小板。

总之，血小板输注是治疗血液病的有效措施之一，本研究结果表明发热及脾大是影响血液病患者血小板输注疗效的不利因素。在血小板输注治疗时，临床医生应充分考虑可能影响输注疗效的因素，如反复多次输血、患者的脾脏大小、感染、发热等，并针对不利因素尽早采取相应的补救措施以提高血小板输注有效率，改善患者预后。

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