改良FLAG方案治疗难治性急性髓细胞白血病的初步分析

我们应用改良及经典FLAG方案治疗16例成人难治性急性髓细胞白血病(AML)，结果报告如下。

1 临床资料与方法

1.1 临床资料

研究对象为2001年5月至2003年5月我院住院的16例成人难治性AML患者。男性10例、女性6例，中位数年龄32岁(17~66)。按FAB分类，16例中 M1 5例，M2 4例，M4 3例，M5 2例，双表型2例。本方案前诱导治疗未达缓解的中位疗程数2个(1~4)，方案包括TA、DA、MA、HA、IDA、VMA、MAE、DAE、HD-MTX、TOAP 、HD-Ara-C(T：吡柔比星；A：阿糖胞苷；D：柔红霉素；M：米托蒽醌；H：三尖杉酯碱；ID：去甲氧柔红霉素；VM：替尼泊甙；E： 依托泊甙；MTX： 甲氨蝶呤；O：长春新碱；P：强的松)。化疗前伴有的预后不良因素有：白血病细胞表达CD34抗原6例，白细胞(WBC)>100×10^9/L 6例，复杂染色体异常2例，多药耐药(MDR)基因阳性3例，骨髓增生异常综合征(MDS)病史1例。

1.2 治疗方法

研究对象随机分为2组。改良组10例接受Ara-C 200 mg/d，VD×5或7 d，化疗前停用G-CSF；经典组6例接受Ara-C 500或1 000 mg/d，VD×5 d，化疗前4~6 h皮下注射G-CSF 300 μg。所有患者使用氟达拉宾50 mg/d，VD×5 d。在化疗后WBC <1.0×10^9/L时应用G-CSF 300 μg/d，皮下注射，至WBC >3.0×10^9/L时停药。每疗程后待WBC恢复接近正常时复查骨髓，按白血病疗效标准评价疗效。

1.3 统计学处理

采用SPSS10.0行χ^2检验。

2 结果

16例成人难治性AML的治疗结果见表1。总的完全缓鲜率(CR) 50%(8/16)，其中改良组的10例患者中7例达CR(70%)，而经典组的6例患者中仅1例达CR(17%)。改良组患者的CR率高于对照组(70% vs 17%)，经卡方检验，卡方值为4.3，P<0.05。改良组化疗后WBC降至最低值(1.4×10^9/L)平均为10 d,中性粒细胞(ANC)回升至0.5×10^9/L以上平均需12 d；化疗后血小板降至最低值(10.5×10^9/L) 平均为8 d，从最低值回升至30×10^9/L以上平均需11 d。经典组化疗后WBC降至最低值(0.7×10^9/L)平均为11 d，ANC回升至0.5×10^9/L以上平均需15 d；化疗后血小板降至最低值(23×10^9/L) 平均为11 d，从最低值回升至30×10^9/L以上平均需20 d。上述指标两组间差异无统计学意义，P >0.05。两组发生肺炎、口腔或上呼吸道感染的感染率分别为50%(5/10)和83%(5/6)，P>0.05，均经抗生素治愈。

表 1 FLAG 方案治疗难治性成人急性髓细胞白血病

Tab.1 FLAG regimen for adult patients with refractory acute myeloid leukemia

	Modified group	Classic group
Cases	10	6
Chemotherapy	DA, TA, MAE, MA, HA, IDA, VDP, VmA	MA, TA, IDA, VmA, VP, TOAP, HA, MAE
Average courses	3.5	3.3
CR	7*	1*
PR	0	2
NR	3	3
Infection	5	5

*P<0.05; CR: Complete remission; PR: Partial remission; NR: NO remission

3 讨论

难治性白血病通常对多种化疗药物产生耐药，治疗非常困难，死亡率极高。目前通常采用的化疗策略是用二线药物联合大剂量的一线药物或联合新药治疗。常用的化疗方案有MA、IA、MAE、DAE、HD- Ara-C和HD-MTX等，其中Ara-C的剂量多在2 000 mg/d×5~6 d，获得的CR率仅有43%~60%[1][2][3][4]，且骨髓抑制和肝损害发生率较高。

氟达拉宾是一种嘌呤类似物，其抗白血病的主要作用机制是通过抑制DNA合成，促进白血病细胞凋亡，还有强烈的免疫抑制作用。先期主要用于治疗慢性淋巴细胞白血病和恶性淋巴瘤，有效率达50%以上，毒副作用小，与Ara-C联合具有强大的协同作用，而且没有交叉耐药发生，近来已较多用于治疗急性白血病和造血干细胞移植的预处理[5]。经典FLAG方案包括Flu 50 mg/d，VD×5 d联合Ara-C 1 000~2 000 mg/d，VD×5 d，化疗前4~6 h皮下注射G-CSF 300 μg/d。为近年治疗难治性AML应用较多的方案之一，总的CR率为 50%~64%[6][7]。骨髓抑制和感染等并发症发生率较高及药物费用昂贵。

本研究对象为16例难治性AML，总的CR率50%，与文献报告基本一致。改良FLAG方案与经典FLAG方案比较，有CR率高、感染率低和节约药物费用等优点，其机制尚不清楚。Estey等[8]报道急性髓系白血病患者化疗时联合应用G-CSF，其疗效明显低于单用化疗药物组。其原因可能是G-CSF刺激白血病细胞的增殖及减低抗癌药物对白血病细胞的致凋亡作用。Schiller等[9]对101例初发AML患者随机分为Ara-C 200 mg/d组(51例)和500 mg/d以上组(50例)，两组CR分别为71%和75%，提示较高剂量Ara-C在诱导治疗方面并不优于200 mg/d组。

本研究初步探讨了治疗难治性AML的适合我国国情的FLAG方案，但因病例数较少，尚需进一步扩大临床研究。

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回结果列表