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血清 IL-2、IL-16 水平的变化和艾滋病患者机会性感染的关系探究 *

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摘要 目的：研究血清 IL-2、IL-16 水平的变化和艾滋病患者机会性感染的关系。**方法：**选择 2016 年 1 月至 2018 年 10 月在我院接受治疗的艾滋病患者 120 例作为观察组，根据美国疾病预防控制中心及世界卫生组织标准将其分为三期，A 期 24 例，B 期 41 例，C 期 55 例，其中 96 例为机会性感染者。同期选择 20 例在本院进行正常体检者作为对照组。观察组采用高效抗逆转录病毒疗法（HAART）治疗。检测和比较各期艾滋病患者与对照组、机会性感染组与非机会性感染组、艾滋病各期治疗前后血清白介素 -2（IL-2）、白介素 -16（IL-16）、$CD4^+$ 细胞、$CD8^+$ 细胞计数的差异。**结果：**观察组各期艾滋病患者血清 IL-2、IL-16 水平明显低于对照组，且 C 期患者血清 IL-2、IL-16 水平均显著低于 A、B 期患者（P<0.05）；观察组及各期患者 $CD4^+$ 细胞计数均低于对照组，$CD8^+$ 细胞计数均高于对照组，且 C 期患者 $CD4^+$ 细胞计数均显著低于 A、B 期患者，$CD8^+$ 细胞计数均高于 A、B 期患者（P<0.05）；机会性感染组患者血清 IL-2、IL-16 水平明显低于非机会性感染组（P<0.05）；治疗后，观察组各期患者血清 IL-2、IL-16 水平较治疗前明显显著升高，且 A 期患者血清 IL-2、IL-16 显著高于 B、C 期患者（P<0.05）。**结论：**艾滋病机会性感染患者血清 IL-2、IL-16 水平均显著降低，通过监测血清 IL-2、IL-16 水平可积极防治机会性感染。

关键词：艾滋病；机会性感染；白介素 -2；白介素 -16

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Relationship between the Levels of serum IL-2 and IL-16 and the Opportunistic Infection in HIV-infected Patients*

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ABSTRACT Objective: To study the relationship between changes of serum il-2 and il-16 and opportunistic infection in AIDS patients. **Methods:** 120 patients with AIDS who received treatment in our hospital from January 2017 to October 2018 were selected as the observation group. According to the standards of the us centers for disease control and prevention and the world health organization, they were divided into three stages: 24 cases of stage A, 41 cases of stage B and 55 cases of stage C, among which 96 cases were opportunistic infection. During the same period, 20 cases of normal physical examination in our hospital were selected as the control group. The observation group was treated with highly active antiretroviral therapy (HAART). To detect and compare the difference of serum interleukin-2 (il-2), interleukin-16 (il-16), $CD4^+$ cells and $CD8^+$ cells between AIDS patients and control group, opportunistic infection group and non-opportunistic infection group before and after treatment of AIDS. **Results:** The levels of serum il-2 and il-16 in the observation group were significantly lower than those in the control group, and the levels of serum il-2 and il-16 in the C group were significantly lower than those in the A and B groups (P<0.05). The $CD4^+$ cell count of the observation group and patients at all stages was lower than that of the control group, and the $CD8^+$ cell count was higher than that of the control group. The $CD4^+$ cell count of patients at stage C was significantly lower than that of patients at stage A and B, and the $CD8^+$ cell count was higher than that of patients at stage A and B (P<0.05). Serum il-2 and il-16 levels in the opportunistic infection group were significantly lower than those in the non-opportunistic infection group(P<0.05). After treatment, serum il-2 and il-16 levels of patients in the observation group were significantly higher than those before treatment, and serum il-2 and il-16 levels of patients in stage A were significantly higher than those in stage B and C (P<0.05). **Conclusion:** Serum il-2 and il-16 levels of AIDS patients with opportunistic infection were significantly reduced, and the monitoring of serum il-2 and il-16 levels can actively prevent and treat opportunistic infection.

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前言

艾滋病是一种因人类免疫缺陷病毒感染所引起的严重免疫性传染性疾病，主要通过性传播、血液传播及母婴传播[1,2]。机体在感染人类免疫缺陷病毒后，患者细胞免疫功能严重受损，导致菌群失调从而发生各种机会性感染。艾滋病患者机会性感染具有多样性、混合性、难治疗性等特点，其诊断困难，预后效果不佳[4]。已有研究表明[5]机会性感染是导致艾滋病患者死亡率增长重要原因之一。因此，及时治疗并采取积极的预防措施可有效减低患者的死亡率。

临床研究认为早期抗病毒治疗艾滋病能够缓解病情，减少机会性感染及肿瘤的发生，而 HAART 是目前较为公认的治疗疗法，对成人儿童均有效。有研究显示经 HAART 治疗的患者 $CD4^+$ 细胞计数及血清 IL-16 水平均显著升高、血清 IL-2 水平则显著降低[6-8]。目前，艾滋病感染患者血清 IL-16 与 IL-2 水平的变化受到关注与重视。本研究旨在探讨血清 IL-2、IL-16 水平的变化和艾滋病患者机会性感染的关系，以期对艾滋病机会性感染的防治找到新的治疗靶点。

1 材料与方法

1.1 一般资料

选择 2016 年 1 月至 2018 年 10 月在我院接受治疗的艾滋病患者 120 例作为观察组，纳入标准：(1)均经过我院艾滋病研究室抗 HIV 初筛选试验，并试验诊断为 HIV 感染者；(2) 符合《HIV/AIDS 诊断标准及处理原则》；(3)患者及其家属知情并签署知情同意书。排除标准：(1)具有抗 HIV 药物史；(2)伴其他恶性肿瘤；(3)具有精神障碍者；(4)处于妊娠期或哺乳期。其中男性患者 103 例，女性患者 17 例，年龄 20~68 岁，平均年龄(40.43± 6.42) 岁。根据世界卫生组织标准将其分为三期，A 期 24 例(血液循环中存在高滴度的游离病毒，可以监测到抗原抗体反应)，B 期 41 例(轻至中度的淋巴结肿大以外，CD4 较高)，C 期 55 例(指 CD4<200)。其中，发生机会性感染患者 96 列。同期选择 20 例在本院进行正常体检者作为对照组，男性 17 例，女性 3 例，年龄 22~63 岁，平均年龄(42.16± 6.04)岁，均无特殊病史，2 个月内无感染史，体检未发现异常。两组患者的年龄、性别等一般资料具有可比性。

1.2 方法

给予观察组患者使用 HAART 治疗，其方案组合均为两个核苷类反转录酶抑制剂及一个非核苷类反转录酶抑制剂。并在治疗前及治疗后第 24 周收集患者 2 mL 血清及抗凝血，经离心处理后，分离血浆以及外周血单核细胞置于 -80℃环境中待检。$CD4^+$ 细胞计数与 $CD8^+$ 计数使用流式细胞仪进行测定，采用 ELISA 双抗体夹心法对血清 IL-2 及 IL-16 进行测定。

1.3 统计学分析

选择 SPSS18.0 进行数据统计，计量资料表示为均数± 标准差($\bar{x}$± s)，采用 t 检验对比，当 P<0.05 时表示其差异在统计学上具有意义。

2 结果

2.1 各期 HIV 患者血清 IL-2、IL-16 水平的变化分析

观察组及各期 HIV 患者血清 IL-2、IL-16 水平明显低于对照组，且 C 期 HIV 患者血清 IL-2、IL-16 水平均显著低于 A、B 期 HIV 患者(P<0.05)，详见表 1。

表 1 各期 HIV 患者血清 IL-2、IL-16 水平的比较($\bar{x}$± s)

Table 1 Comparison of the serum IL-2, IL-16 levels between the HIV patients at different stage($\bar{x}$± s)

Groups	n	IL-2(pg/mL)	IL-16(ng/mL)
Observation group	120	60.32± 10.43[a]	243.42± 36.43[a]
Stage A	24	73.42± 13.74[abc]	265.32± 30.16[abc]
Stage B	41	68.21± 10.43[ab]	230.47± 28.64[ab]
Stage C	55	50.17± 8.43[a]	175.89± 26.75[a]
Control group	20	114.53± 24.13	510.64± 56.84

Note: Compared with the control group, [a]P＜0.05; Compared with the Stage C; [b]P＜0.05. Compared with the Stage B, [c]P＜0.05.

2.2 各期 HIV 患者 $CD4^+$ 细胞、$CD8^+$ 细胞计数变化分析

观察组及各期 HIV 患者 $CD4^+$ 细胞计数均低于对照组，$CD8^+$ 细胞计数均高于对照组，且 C 期 HIV 患者 $CD4^+$ 细胞计数均显著低于 A、B 期 HIV 患者，$CD8^+$ 细胞计数均高于 A、B 期 HIV 患者，详见表 2。

2.3 机会性感染组与非机会性感染组血清 IL-2、IL-16 水平比较

机会性感染组患者血清 IL-2、IL-16 水平明显低于非机会性感染组(P<0.05)，详见表 3。

2.4 各期 HIV 患者治疗前后血清 IL-2、IL-16 水平的变化比较

治疗后，各期患者血清 IL-2、IL-16 水平较治疗前明显升高，且 A 期患者血清 IL-2、IL-16 显著高于 B、C 期患者(P<0.05)，详见表 4。

3 讨论

艾滋病是一种难以治愈且危害性极大的慢性传染病，由感染 HIV 病毒引起[9,10]，HIV 能攻击人体免疫系统[11,12]，而 $CD4^+$ 细

胞则为主要攻击目标,HIV 通过大量破坏该细胞，导致丧失免疫功能,通常合并多种机会性感染。机会性感染是危险艾滋病患者生命健康安全的重要因素。有关研究指出[13-16],艾滋病患者并非因为感染人类免疫缺陷病毒后直接死亡,通常是因并发了其他疾病而致死,其中机会性感染则为最主要的死亡原因。

表 2 各期 HIV 患者 $CD4^+$ 细胞、$CD8^+$ 细胞水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the $CD4^+$ cell, $CD8^+$ cell between the HIV patients at different stage($\bar{x}\pm s$)

Groups	n	$CD4^+$(× 10^6/L)	$CD8^+$(× 10^6/L)
Observe group	120	362.84± 145.32[a]	704.83± 210.62[a]
Stage A	24	452.32± 163.93[abc]	597.13± 197.32[abc]
Stage B	41	396.41± 139.87[ab]	711.32± 268.13[ab]
Stage C	55	237.19± 176.33[a]	769.13± 301.51[a]
Control group	20	772.32± 175.86	581.93± 107.93

Note: Compared with the control group, [a]P＜0.05; Compared with the Stage C; [b]P＜0.05. Compared with the Stage B, [c]P＜0.05.

表 3 机会性感染组与非机会性感染组血清 IL-2、IL-16 水平比较($\bar{x}\pm s$)

Table 3 Comparison the serum IL-2, IL-16 levels between Opportunistic infections group and Non-opportunistic infections group($\bar{x}\pm s$)

Groups	n	IL-2(pg/mL)	IL-16(ng/mL)
Opportunistic infections group	96	52.32± 9.32[a]	178.43± 30.08[a]
Non-opportunistic infections group	24	67.15± 11.73	236.19± 29.64

Note: Compared with the Non-opportunistic infections group, [a]P＜0.05.

表 4 各期 HIV 患者治疗前后血清 IL-2、IL-16 水平比较($\bar{x}\pm s$)

Table 4 Comparison the serum IL-2, IL-16 levels between the three groups before and after treatment($\bar{x}\pm s$)

Groups	n	IL-2(pg/mL)		IL-16(ng/mL)	
		Before treatment	After treatment	Before treatment	After treatment
Stage A	24	73.42± 13.74[a]	86.43± 16.43[bc]	265.32± 30.16[abc]	353.83± 35.64[bc]
Stage B	41	68.21± 10.43[a]	78.17± 15.32[bc]	230.47± 28.64[ab]	248.16± 25.32[bc]
Stage C	55	50.17± 8.43[a]	56.98± 10.43	175.89± 26.75[a]	193.43± 24.46

Note: Compared with After treatment, [a]P＜0.05; Compared with the Stage C, [b]P＜0.05. Compared with the Stage B, [c]P＜0.05.

研究表明[17,18]机会性感染的发生与病原菌的毒力以及患者的免疫水平直接相关，而 $CD4^+$ 细胞计数是机体免疫状态最直观的体现,其与机会性感染发生有密切的关系。研究显示[19],在 $CD4^+$ 细胞计数低于 500 个 mm^3 时,会发生结合以及其他细菌感染;在 $CD4^+$ 细胞计数低于 500 个 mm^3 使,会发生结合以及其他细菌感染[20];在 $CD4^+$ 细胞计数低于 200 个 mm^3 时,1 年后发生机会性感染的概率高达 30%以上,2 年后发生概率可到 55%以上[21]。且本次研究结果显示 B、C 期患者机会性感染几率更高。临床研究显示艾滋病机会性感染可发生于机体任何部位和组织器官,并且可有多个组织器官受累,也可有数种机会性感染同时存在。由于艾滋病机会性感染表现较为复杂且不典型性,导致诊断较为困难,导致许多患者都是在症状表现明显时才入院就诊,而此时病情通常已进入到了晚期,错过了治疗的最佳时间，因此对于艾滋病机会性感染患者尽早采取积极有效的预防措施,及时治疗,对提高患者生存率具有重要的临床意义。

目前对于艾滋病感染研究最多及最重要的则为 T 淋巴细胞,不同的淋巴细胞在激活时会产生不同的细胞因子,因此所发挥的作用也各不相同。IL-16 又被称为淋巴细胞趋化因子,可通过 $CD8^+$T 细胞[21]。肥大细胞等产生,但主要由 $CD8^+$T 淋巴细胞分泌,属于一种分泌型糖蛋白。已有研究显示[22],血清 IL-16 高水平表示 HIV 低复制及病情的好转。本研究结果中,艾滋病患者血清 IL-16 水平明显低于正常者，且 A 期患者高于 B、C 期患者,B 期患者高于 C 期患者;本次研究结果显示 B、C 期患者血清 IL-16 水平则显著低于 A 期患者,且患者经 HAART 治疗后,其血清 IL-16 水平显著升高,分析原因可能与患者 HIV 病毒载量较低有关。通过查阅文献,我们推测 IL-16 与 CD4 相结合后，可启动 HIV-1 的活性以及抑制 mRNA 的表达。Caufour P 等学者认为[23]IL-16 抑制 HIV 复制是阻滞 HIV 病毒后的一个表达步骤。Bader A 等学者则认为与机体的免疫重建有关,淋巴因子的治疗方法相当于是一种补偿式的处理,对一些重要的免疫功能有一定的恢复作用，因此抑制了 HIV 的扩散以及 HIV 感染对免疫系统的影响[24]。由此可见,IL-16 可作为艾滋病机会性感染的病情观察指标。

IL-2 为γ链细胞因子,对免疫反应的正常功能及对增强抗感染免疫应答有重要作用，因此 IL-2 被广泛用于抗病毒的辅助治疗,近几年逐渐试用于抗 HIV 感染[25-27]。IL-2 是一种抗原活性 T 细胞及自然杀伤细胞存活以及增殖所必需的细胞因子,可促进细胞分泌及分化功能[28-30]。本研究结果显示 B、C 期患者

血清 IL-2 水平明显低于 A 期患者，且随着病情的进展，其水平则逐渐下降；机会性感染患者血清 IL-2 水平则显著低于非机会性感染患者，且患者经 HAART 治疗后，其血清 IL-2 水平显著升高。本研究结果显示患者治疗后 $CD4^+$ 细胞计数明显增加，可见 IL-2 与 $CD4^+$ 细胞计数呈正相关，提示 IL-2 可能调节 T 细胞功能[31]。

综上所述，艾滋病机会性感染患者血清 IL-2、IL-16 水平均显著降低，通过监测血清 IL-2、IL-16 水平可能有助于预防机会性感染，从而及时识别治疗，降低患者死亡率。

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