doi: 10.13241/j.cnki.pmb.2019.22.011

肺结核患者血清 IFN-γ、Il-1β 和 TNF-α 水平的临床检测价值分析 *

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摘要 目的:研究肺结核患者血清 γ 干扰素(IFN-γ)、白介素 -1β(Il-1β)以及肿瘤坏死因子 -α(TNF-α)水平的临床检测价值。**方法:**选择 2015 年 1 月～2018 年 12 月在北京市顺义区医院治疗的 25 例肺结核患者作为肺结核组,并且选择同期在该院进行体检的 25 例健康人作为对照组。采用酶联免疫吸附法(ELISA)检测并且比较肺结核组以及对照组研究对象的血清 IFN-γ、Il-1β 和 TNF-α 水平,比较痰菌阴性组(n=14 例)以及痰菌阳性组(n=11 例)、无空洞组(n=15 例)以及有空洞组(n=10 例)的血清 IFN-γ、Il-1β、TNF-α 水平。**结果:**肺结核组患者的血清 IFN-γ、Il-1β、TNF-α 水平均明显高于对照组(P<0.05);痰菌阳性组肺结核患者的血清 IFN-γ、Il-1β、TNF-α 水平均明显高于痰菌阴性组患者(P<0.05);有空洞组肺结核患者的血清 IFN-γ、Il-1β、TNF-α 水平均明显高于无空洞组患者(P<0.05)。**结论:**肺结核患者的血清 IFN-γ、Il-1β 和 TNF-α 水平明显高于健康者,有助于判断疾病进程,这些细胞因子可能在结核病的发病中发挥着重要的作用。

关键词:肺结核;γ 干扰素;白介素 -1β;肿瘤坏死因子 -α;检测价值

中图分类号:R521 **文献标识码:**A **文章编号:**1673-6273(2019)22-4257-04

Clinical Value of Serum IFN-gamma, Il-1beta and TNF-alpha Levels for the Patients with Pulmonary Tuberculosis*

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ABSTRACT Objective: To study the clinical value of serum interferon-gamma (IFN-gamma), interleukin-1beta (Il-1beta) and tumor necrosis factor-alpha (TNF-alpha) levels in patients with pulmonary tuberculosis. **Methods:** 25 tuberculosis patients treated in Shunyi District Hospital of Beijing from January 2015 to December 2018 were selected as the tuberculosis group, and 25 healthy people who underwent physical examination in the hospital during the same period were selected as the control group. The serum levels of IFN-gamma, Il-1beta and TNF-alpha in tuberculosis group and control group were detected and compared by ELISA. The serum levels of IFN-gamma, Il-1beta and TNF-alpha in sputum negative group (n=14 cases) and sputum positive group (n=11 cases), non-cavity group (n=15 cases) and cavity group (n=10 cases) were compared. **Results:** The serum levels of IFN-gamma, Il-1beta and TNF-alpha in tuberculosis group were significantly higher than those in control group (P < 0.05). The serum levels of IFN-gamma, Il-1beta and TNF-alpha in sputum positive group were significantly higher than those in sputum negative group (P < 0.05). The serum levels of IFN-gamma, Il-1beta and TNF-alpha in patients with pulmonary tuberculosis in the cavity group were significantly higher than those in the non-cavity group (P < 0.05). **Conclusion:** The serum levels of IFN-gamma, Il-1beta and TNF-alpha in patients with pulmonary tuberculosis were significantly higher than those in healthy people. These cytokines may help to judge the course of disease and play an important role in the pathogenesis of tuberculosis.

Key words: Tuberculosis; Interferon gamma; Interleukin-1beta; Tumor necrosis factor-alpha; Clinical value of detection

Chinese Library Classification(CLC): R521 Document code: A

Article ID: 1673-6273(2019)22-4257-04

前言

结核病是由于结核分枝杆菌感染而导致的一种慢性传染性疾病,能发病于在机体的多个器官中,其中最为多见的是肺部发病,临床上称为肺结核[1-3]。结核病目前仍是影响全世界公众生命健康的一种严重的致死性疾病,每年由于结核病而死亡

* 基金项目:北京市教委科技计划重点项目 (KZ201810025033)

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(收稿日期:2019-03-07 接受日期:2019-03-29)

的患者人数高达 130 万例[4,5]，而我国的结核病感染人数位居世界首位。细胞因子是由丝裂原、免疫原或者其他的刺激剂诱导多种细胞生成的具有可溶性以及低分子量特点的蛋白质，在血细胞生成、适应性免疫以及固有免疫的调节、损伤组织的修复、细胞的生长等多种生物过程中发挥着重要的作用[6-9]。

近年来，有关细胞因子在肺结核发病机制中的临床研究不断增多，引起了广泛的重视[10]。多种细胞因子均被证实在肺结核的免疫应答以及免疫发病过程种发挥着重要的功能。其中，Th1 细胞分泌的 γ 干扰素(IFN-γ)等细胞因子可以有效参与细胞免疫过程，白介素 -1β(Il-1β)以及肿瘤坏死因子 -α(TNF-α)作为前炎症细胞因子，在肺结核的免疫病理过程中具有重要的作用。本研究主要比较分析了不同肺结核患者的血清 γ 干扰素(IFN-γ)、白介素 -1β(Il-1β)以及肿瘤坏死因子 -α(TNF-α)水平，旨在明确血清 IFN-γ、Il-1β 和 TNF-α 水平检测对肺结核患者的临床应用价值。

1 资料与方法

1.1 一般资料

选择 2015 年 1 月～2018 年 12 月在北京市顺义区医院治疗的 25 例肺结核患者作为肺结核组，纳入标准：年龄 16～68 岁；符合肺结核的诊断标准；空腹血糖值小于 6. 0 mmol/L；肝肾功能均比较正常；对本项研究均知晓并签订了同意书。排除标准：合并有肝、代谢、肾以及自身免疫性疾病，血液系统以及内分泌有严重疾病者；恶性肿瘤患者；有精神病病史、患有神经系统疾病患者；同时在参加其他研究项目的患者。肺结核组 25 例，男 14 例，女 11 例；年龄 <20 岁者 1 例，20～39 岁者 5 例，40～59 岁者 11 例，≥ 60 岁者 8 例，平均年龄(43.92± 11.54)岁；无空洞者 15 例，有空洞者 10 例；痰菌阴性者 14 例，痰菌阳性者 11 例；病灶范围：病变占据 1～2 肺野者 7 例，占据 3～4 肺野者 13 例，占据 5～6 肺野者 5 例。同期在该院进行体检的 25 例健康人作为对照组。对照组 25 例，男 13 例，女 12 例；年龄 <20 岁者 2 例，20～39 岁者 10 例，40～59 岁者 11 例，≥ 60 岁者 2 例，平均年龄(39.72± 10.15)岁。

1.2 研究方法

① 肺结核组以及对照组均于清晨空腹抽取 3 mL 静脉血，使用 ELISA 法检测三组的血清 IFN-γ、Il-1β 和 TNF-α 水平，试剂盒分别购自成都安普诺生物科技有限公司，北京普华仕科技发展有限公司，武汉伊莱瑞特生物科技股份有限公司。比较肺结核组和对照组的血清 IFN-γ、Il-1β、TNF-α 水平。

② 根据肺结核组患者的痰菌结果分为痰菌阴性组(n=14 例)以及痰菌阳性组(n=11 例)，检测并且比较痰菌阴性组以及痰菌阳性组的血清 IFN-γ、Il-1β、TNF-α 水平。

③ 根据肺结核组患者有无空洞而分为无空洞组 (n=15 例)以及有空洞组(n=10 例)，检测并且比较无空洞组和有空洞组的血清 IFN-γ、Il-1β、TNF-α 水平。

1.3 统计学分析

采用 SPSS 22.0 对数据进行统计学分析，两组间计量资料对比用 t 检验，计数资料用 x^2 检验，P<0.05 为差异有统计学意义。

2 结果

2.1 肺结核组和对照组的血清 IFN-γ、Il-1β、TNF-α 水平比较

肺结核组患者的血清 IFN-γ、Il-1β、TNF-α 水平均明显高于对照组(P<0.05)，见表 1。

表 1 肺结核组和对照组的血清 IFN-γ、Il-1β、TNF-α 水平比较($\bar{x} \pm s$)

Table 1 Comparison of the serum IFN-gamma, Il-1beta and TNF-alpha levels between tuberculosis group and control group ($\bar{x} \pm s$)

Groups	n	IFN-γ (ng/L)	Il-1β (ng/L)	TNF-α (ng/L)
Control group	25	11.38 ± 2.56	0.79 ± 0.32	14.36 ± 1.25
Pulmonary tuberculosis group	25	42.78 ± 10.14*	1.24 ± 0.73*	59.73 ± 12.46*

Note: Compared with the control group, *P<0.05.

2.2 痰菌阴性组和痰菌阳性组的血清 IFN-γ、Il-1β、TNF-α 水平比较

痰菌阳性组肺结核患者的血清 IFN-γ、Il-1β、TNF-α 水平均明显高于痰菌阴性组患者(P<0.05)，见表 2。

表 2 痰菌阴性组以及痰菌阳性组的血清 IFN-γ、Il-1β、TNF-α 水平比较($\bar{x} \pm s$)

Table 2 Comparison of the serum IFN-gamma, Il-1beta and TNF-alpha levels in sputum negative group and sputum positive group($\bar{x} \pm s$)

Groups	n	IFN-γ (ng/L)	Il-1β (ng/L)	TNF-α (ng/L)
Sputum negative group	14	34.29 ± 7.51	1.13 ± 0.45	55.43 ± 10.78
Sputum positive group	11	45.63 ± 12.74*	1.36 ± 0.87*	62.17 ± 10.35*

Note: Compared with the sputum negative group, #P<0.05.

2.3 无空洞组和有空洞组的血清 IFN-γ、Il-1β、TNF-α 水平比较

有空洞组肺结核患者的血清 IFN-γ、Il-1β、TNF-α 水平均明显高于无空洞组患者(P<0.05)，见表 3。

3 讨论

根据结核病患者结核菌感染的状态，可将人群分成活动性结核、无结核感染、治愈以及潜伏性结核[11-13]。肺结核作为一种免疫相关性传染疾病，巨噬细胞和 T 淋巴细胞介导的免疫反应均参与结核病的免疫发病过程和免疫应答，多种细胞因子在该病的发生以及发展过程中有着重要的作用[14-17]。研究表明肺结

表 3 无空洞组和有空洞组的血清 IFN-γ、Il-1β、TNF-α 水平比较($\bar{x} \pm s$)

Table 3 Comparison of serum IFN-gamma, Il-1beta and TNF-alpha levels between non-empty group and empty group ($\bar{x} \pm s$)

Groups	n	IFN-γ (ng/L)	Il-1β (ng/L)	TNF-α (ng/L)
Non-empty group	15	36.72 ± 8.34	0.76 ± 0.31	53.29 ± 10.14
Empty group	10	46.29 ± 11.48^{+}	1.23 ± 0.74^{+}	61.38 ± 11.78^{+}

Note: Compared with the non-empty group, $^{+}P<0.05$.

核作为一种迟发型的细胞免疫疾病，患者受到结核菌感染后，会对机体的免疫细胞产生特异性刺激，释放出 IFN-γ、TNF-α 和 IL-2 等多种细胞因子[18]。本研究结果显示肺结核组患者的血清 IFN-γ、Il-1β、TNF-α 水平均明显高于对照组，提示这些细胞因子可能在结核病的发病中发挥着重要的作用。

IFN-γ 是一种由 Th1 细胞分泌产生的免疫调节细胞因子，可以有效激活单核细胞，促使单核细胞积聚于肺结核患者的病灶周围，从而抑制感染进一步的扩散，促进结核肉芽肿的形成，而且可以使巨噬细胞的杀菌效果得到明显的增强，在抗结核免疫中发挥着极为重要的效果[19-22]。IFN-γ 在细胞免疫以及体液免疫过程中均具有免疫调节功能，而且对 NK 细胞和巨噬细胞有一定程度的免疫增强效果[23,24]。本研究结果显示痰菌阳性组肺结核患者的血清 IFN-γ 水平均明显高于痰菌阴性组患者，有空洞组肺结核患者的血清 IFN-γ 水平均明显高于无空洞组患者，提示表明肺结核患者的血清 IFN-γ 水平可能与病情的轻重程度相关性，当肺结核患者的病情比较严重时，机体会生成更多的 IFN-γ，以进一步参与抗结核免疫过程。

IL-1β 是一种与细胞凋亡具有紧密相关性的炎症细胞因子，在机体受到结核分枝杆菌感染的过程中，巨噬细胞会大量分泌 IL-1β，而成熟的 IL-1β 又能使凋亡相关蛋白 caspase-1 的活性明显增强[25-27]。本研究结果显示痰菌阳性组肺结核患者的血清 Il-1β 水平均明显高于痰菌阴性组患者，有空洞组肺结核患者的血清 Il-1β 水平均明显高于无空洞组患者，提示随着肺结核患者病情的加重，大量的 Il-1β 及其介导的信号通路会在结核保护性免疫中发挥重要的作用。

TNF-α 是一种由淋巴细胞以及单核巨噬细胞生成的前炎症细胞因子，能促进巨噬细胞发生活化，使巨噬细胞的吞噬作用明显增强，有效限制肉芽肿的形成以及结核菌的扩散，激活其他细胞因子，造成炎症细胞发生大量聚集[28,29]；上调黏附分子的表达水平，明显增加异型细胞以及同型细胞之间的黏附作用，在肉芽组织的生成长中发挥着重要的作用[30]。但是，TNF-α 也能造成肺结核患者空洞形成以及组织坏死。有研究显示有空洞的肺结核患者的支气管冲洗液中检测到的 TNF-α 表达水平显著高于无空洞的肺结核患者。本研究结果显示痰菌阳性组肺结核患者的血清 TNF-α 水平均明显高于痰菌阴性组患者，有空洞组肺结核患者的血清 TNF-α 水平均明显高于无空洞组患者。导致该种现象发生的原因可能是血清 TNF-α 水平的明显升高会对肺结核患者产生一定程度的免疫保护效果，但是出现空洞的肺结核患者机体生产的血 TNF-α，因为受到隔室化作用的影响而大多数被局限于肺部。由于不同肺结核患者血清 IL-6、IL-12、IL-23、TNF-α、IFN-γ 表达水平具有明显的差异，有助于判断肺结核的发展进程，与 Bini E I[31]的研究结果相一致。

综上所述，肺结核患者的血清 IFN-γ、Il-1β 和 TNF-α 水平明显高于健康者，这些细胞因子可能在结核病的发病中发挥着重要的作用，有助于判断疾病进程，应重视其检测价值。

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