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糖尿病合并肺结核患者诱导耐药性危险因素的回归分析

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摘要 目的:研究 2 型糖尿病(Type 2 Diabetes, T2DM)合并肺结核(Tuberculosis, TB)患者诱导耐药性危险因素的回归分析。**方法:**从 2012 年 3 月到 2013 年 3 月,于我院共计有 124 例患者被确诊为肺结核,将其作为研究对象。根据患者是否合并有 2 型糖尿病,将其分成观察组(49 例)及对照组(75 例)。对全部患者进行耐药性实验,分别经单因素分析及 Logistic 回归性分析寻找诱导耐药性的危险因素。**结果:**观察组在治疗过程中断、有吸烟习惯、依从性差、病程 ≥ 1 年、HbA1c 值 $\geq 6.5\%$ 等方面所占比例显著高于对照组,差异均有统计学意义(均 $P < 0.05$)。由多因素分析可知,治疗过程中断、有吸烟习惯、依从性差、病程 ≥ 1 年、HbA1c 值 $\geq 6.5\%$ 等均为糖尿病合并肺结核患者的危险因素。**结论:**T2DM 合并 TB 患者诱导耐药性的危险因素较多,临床应重点关注,并采取相应措施,从而为临床治疗提供更为有利的条件。

关键词:糖尿病;肺结核;耐药性;危险因素;回归分析

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Regression analysis of risk factors of induced drug resistance in patients of Type 2 Diabetes combined with tuberculosis

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ABSTRACT Objective: To study risk factors of induced drug resistance in patients of Type 2 Diabetes combined with tuberculosis through regression analysis. **Methods:** 124 patients who were diagnosed with TB from March 2012 to March 2013 in our hospital were selected as a research object. Patient with type 2 diabetes were divided into 2 groups, those who were with tuberculosis were in observation group (49 cases) while the rest were in control group (75 cases). All patients were subjected to the drug resistance experiments. Single factor analysis and logistic regression analysis were used for the test of risk factors of induced drug resistance respectively. **Results:** In observation group, the occurrences of treatment interruption, smoking habits, poor compliance, duration ≥ 1 -year, HbA1c values $\geq 6.5\%$ were significantly higher, and the differences were statistically significant ($P < 0.05$). According to the multivariate analysis, the treatment interruption, smoking habits, poor compliance, duration ≥ 1 -year, HbA1c values $\geq 6.5\%$, were risk factors in diabetic patients with pulmonary tuberculosis's risk factors. **Conclusion:** There are quite a number of risk factors for inducing drug resistance in patients with T2DM combined TB. More attention and measures should be taken so that more favorable conditions for clinical treatment can be provided.

Key words: Diabetes; Tuberculosis; Resistance; Risk factors; Regression analysis

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前言

伴随我国人民生活水平的提高, T2DM 疾病发病率亦不断增加。而 TB 是一种全球性公共卫生的问题, 由于近年来 TB 防治工作的有效进展, 我国 TB 疾病已受到较好控制^[1]。然而, 有研究报道称^[2], T2DM 患者在各类原因的作用下, TB 发生率甚至显著高于非 T2DM 群体, 同时, TB 的存在常常加重了 T2DM 患者的病情。此种现象在临床造成了较大影响, 诸多学者逐渐开始研究 T2DM 患者合并 TB 疾病的发病危险因素, 亦取得了较大进展^[3]。国外 Chung WS 等人^[4]报道称, 单纯研究发病的危险因素尚不能完全从根本上解决治疗难点, 而因继续探

索, 寻找更为深入的内在机理。国内对此方面报道较少, 鉴于此, 本文即通过研究 T2DM 合并 TB 疾病患者诱导耐药性的有关危险因素, 并进行分析, 得到了一些结论, 现报道如下。

1 资料和方法

1.1 临床资料

从 2012 年 3 月到 2013 年 3 月, 于我院共计有 124 例患者被确诊为肺结核, 将其作为研究对象。其中男 72 例, 女 52 例。年龄在 29 至 56 岁间, 平均年龄为 48.6 ± 7.7 岁。根据患者是否合并有 2 型糖尿病, 将其分成观察组(49 例)及对照组(75 例)。其中观察组含男 29 例, 女 24 例, 男女比为 1.208。年龄在 29 至 53 岁间, 平均年龄为 48.2 ± 5.8 岁。对照组含男 43 例, 女 32 例, 男女比为 1.344。年龄在 30 至 56 岁间, 平均年龄为 48.9 ± 4.5 岁。两组在性别比例和年龄以及肺结核病情等方面对比, 差异无统计学意义($P > 0.05$)。具有可比性。

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1.2 纳入标准

(1)符合 2001 版《肺结核诊断和治疗指南》中关于肺结核疾病的诊断标准^[5];(2)符合糖尿病的诊断标准^[6]。(3)病程 ≥ 1 年,2 型糖尿病的诊断时间先于肺结核疾病的一年以上。(4)患者痰培养及药敏实验均显示为阳性。

1.3 排除标准

(1)合并有感染性病症者;(2)对抗结核类药物过敏者;(3)有严重的心、肺、肝、肾等器官性功能不全者;(4)合并有恶性肿瘤及血液类疾病者。

1.4 观察指标

(1)居住地点:城市 / 农村;(2)居住条件:好 / 差;(3)治疗过程:持续 / 中断;(4)吸烟习惯:有 / 无;(5)依从性:好 / 差;(6) 病程: < 1 年 / ≥ 1 年;(7)HbA1c 值: < 6.5% / $\geq 6.5\%$;(8) BMI 值: < 25 / ≥ 25 ;(9)高脂血症:合并 / 不合并。

1.5 耐药性试验

全部患者均于晨间取其痰液 5ml 检查,接种改良的 Roch 型培养基,有关培养步骤依照中国的防痨协会制定的《结核病诊断实验室检验规程》^[7]实施结核分支杆菌的培养。若结核菌株为阳性,则予以菌型鉴定,分离菌株实施药敏试验。其中质量控制以 HRV37 药敏株作为对照。

1.6 统计学方法

采用 SPSS13.0 统计软件分析,计数资料比较采用 χ^2 检验,计量资料以($\bar{x} \pm s$)表示,实施 t 检验。多因素分析以 Logistic 法行回归性分析。P<0.05 为差异有统计学意义。

2 结果

2.1 两组诱导耐药性单因素情况对比

观察组在治疗过程中断、有吸烟习惯、依从性差、病程 ≥ 1 年、HbA1c 值 $\geq 6.5\%$ 等方面所占比例显著高于对照组,差异均有统计学意义(均 P<0.05)。见下表 1:

表 1 两组诱导耐药性单因素情况对比(例, $\bar{x} \pm s$)
Table 1 Comparison of single factors of induction of drug resistance(n, $\bar{x} \pm s$)

因素 Factor	观察组(n=49) Observation group	对照组(n=75)Control group	χ^2 值 χ^2 Value	P 值 P Value
居住地点 Tempat tinggal				
城市 City	13(26.53)	28(37.33)	1.563	0.211
农村 Country	36(73.47)	47(62.67)		
居住条件 Housing conditions				
好 Good	8(16.33)	20(26.67)	1.813	0.178
差 Bad	41(83.67)	55(73.33)		
治疗过程 Therapeutic process				
持续 Abidance	10(20.41)	29(38.67)	4.583	0.032
中断 Interruption	39(79.59)	46(61.33)		
吸烟习惯 Smoking habit				
有 Yes	34(69.39)	34(45.33)	6.924	0.009
无 No	15(30.61)	41(54.67)		
依从性 Compliance				
好 Good	5(10.20)	49(65.33)	36.640	0.000
差 Bad	44(89.80)	26(34.67)		
病程 Course of disease				
< 1 年 Less than 1 year	12(24.49)	37(49.33)	7.653	0.006
≥ 1 年 More than 1 year	37(75.51)	38(50.67)		
HbA1c 值 HbA1c value				
< 6.5%	9(18.37)	45(60.00)	20.896	0.000
$\geq 6.5\%$	40(81.63)	30(40.00)		
BMI 值 BMI Value				
< 25	35(71.43)	57(76.00)	0.323	0.570
≥ 25	14(28.57)	18(24.00)		
高脂血症 Hyperlipemia				
合并 Combined	11(22.45)	25(33.33)	1.704	0.192
不合并 Not combined	38(77.55)	50(66.67)		

2.2 诱导耐药性的多因素 Logistic 回归性分析

由多因素分析可知,治疗过程中断、有吸烟习惯、依从性差、

病程≥ 1 年、HbA1c 值≥ 6.5%等均为糖尿病合并肺结核患者的危险因素。见下表 2:

表 2 诱导耐药性的多因素 Logistic 回归性分析(例, $\bar{x} \pm s$)

Table 2 Multivariate Logistic regression analysis of risk factors of induced drug resistance ($n, \bar{x} \pm s$)

危险因素 Risk factors	β 值 β Value	标准误 S.E	OR 值 OR Value	P 值 P Value	95%CI	
					下限 Lower limit	上限 Upper limit
治疗过程中断 Treatment interruption	0.282	0.128	1.326	0.020	1.032	1.704
病程≥ 1 年 Duration ≥ 1 -year	0.231	0.114	1.260	0.024	1.008	1.575
依从性差 Poor compliance	0.895	0.214	2.447	0.002	1.609	3.723
有吸烟习惯 Smoking habits	0.812	0.312	2.252	0.000	1.222	4.152
HbA1c 值≥ 6.5% HbA1c values ≥ 6.5%	0.921	0.105	2.512	0.004	2.045	3.086

3 讨论

在临床上,T2DM 合并 TB 患者通常病情较重,因 T2DM 患者代谢紊乱致使机体抵抗力减弱,在感染结核菌之后较易发病,病情迅速恶化,主要表现在肺结核症状起病隐匿^[7]。且病变累及范围较广,组织破坏能力较强,还可形成干酪坏死及空洞,以及咯血致死等现象,对临床治疗产生一定困难,预后与单纯的 TB 患者相比较差,国内外亦逐渐开始重视此类合并症状的治疗^[8]。

对于 T2DM 合并 TB 疾病的发病机理,国外 Jurcev-Savicevic A 等人^[9] 报道称,可能与患者机体防御能力较低有关,T2DM 患者机体中性粒细胞的趋化和吞噬,以及杀菌作用下降,且血糖及组织内糖水平含量上升,利于结核菌生长繁殖,加之患者脂肪代谢亦有障碍,促使血游离脂肪酸及甘油三酯水平上升,亦为结核菌繁殖营造了营养环境^[10]。此外,T2DM 患者由于脂肪代谢异常,转化为脂溶性的维生素 A 的机能下降,促使维生素 A 含量缺乏,降低呼吸道粘膜的上皮对于外界感染情况的抵抗能力,加速结核菌感染^[11]。

据有关统计^[12],T2DM 患者发生肺结核的比例约为非 T2DM 患者的 3 倍,随之出现的耐药性情况亦逐渐增多,临床上对于研究 T2DM 合并 TB 患者发生耐药性的危险因素较为重视,然而对于 T2DM 合并 TB 患者诱导形成耐药性的有关危险因素则鲜有报道,本文即对此展开研究,以期临床治疗提供一些理论依据。

笔者在研究后发现,T2DM 合并 TB 的观察组在治疗过程中断、有吸烟习惯、依从性差、病程≥ 1 年、HbA1c 值≥ 6.5%等方面所占比例显著高于对照组,且经 Logistic 回归性分析后,上述 5 个因素均为诱导形成耐药性的有关危险因素。其中,在治疗过程中断及依从性差等方面,国外临床研究亦证实实施全程及规则性治疗可视为避免结核杆菌形成耐药性的一种根本性措施,而与之相反的治疗过程有所中断及用药依从性较差等不规律治疗均为诱发耐药的危险因素^[13]。在病程≥ 1 年方面,可

能因多次予以多类抗结核药物,同时有上述不规则用药等情况,极易产生耐药性,由此可知,T2DM 合并 TB 患者应尽早治疗^[14]。在吸烟习惯方面,长期大量的吸烟不仅对机体细胞免疫的功能产生干扰,还可损伤患者呼吸道有关上皮细胞,从而抑制其肺功能,降低机体抵抗力,并影响药物疗效,使机体结核杆菌产生耐药性^[15]。Jali MV 等人^[16]亦报道称,T2DM 合并 TB 患者人群中吸烟比例和耐药性呈正相关。因此需积极戒烟。在 HbA1c 值方面,由于该值可反映患者机体 120d 血糖的控制水平,HbA1c 水平过高则意味着血糖控制能力较差,而机体中血糖水平过高,容易使组织产生胰岛素抵抗现象,葡萄糖的无氧代谢变强,乳酸和酮体发生蓄积形成酸性环境,促进结核杆菌的生长^[17]。而国外 Babalik A 等人^[18-19]报道表明,糖化血红蛋白的水平过高易形成低氧血症,导致肺部局部出现缺血缺氧症状,结核杆菌因此而更利于生存。因此确保血糖水平处于稳定平衡,可有效降低耐药性^[20]。

综上所述,T2DM 合并 TB 患者诱导耐药性的危险因素较多,临床应重点关注,并采取相应措施,从而为临床治疗提供更为有利的条件。

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