

空腹血糖与间质性肺疾病关系研究

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摘要

目的: 探讨高血糖是否为间质性肺疾病危险因素, 以及高血糖是否导致间质性肺疾病患者预后不良。方法: 收集青岛大学附属医院2019年1月~2019年12月住院患者病例资料, 间质性肺疾病者为实验组(150例), 无间质性肺疾病者为对照组(300例), 比较两组患者空腹血糖是否存在差异; 将间质性肺疾病患者按空腹血糖分为高血糖组(51例)和正常血糖组(99例), 比较两组患者血气分析、六分钟步行距离、肺功能、住院时长、死亡率等预后指标。结果: 1) 间质性肺疾病组空腹血糖水平明显高于无间质性肺疾病组($p < 0.05$)。2) 高血糖组与正常血糖组比较, 氧分压、二氧化碳分压、氧饱和度、FVC、FEV1、DLCO、PEF、住院时长、死亡率, 差异具有统计学意义($p < 0.05$); 年龄、BMI、六分钟步行距离, 差异无统计学意义($p > 0.05$)。3) 皮尔逊相关分析结果显示, 空腹血糖水平与住院时长($r = 0.232, p < 0.05$)呈正相关, 与氧分压($r = -0.311, p < 0.05$)、氧饱和度($r = -0.255, p < 0.05$)、FVC ($r = -0.312, p < 0.05$)、FEV1 ($r = -0.301, p < 0.05$)、DLCO ($r = -0.222, p < 0.05$)、PEF ($r = -0.627, p < 0.05$)呈负相关。结论: 高血糖可致使肺部受损, 是导致ILD的独立危险因素之一。ILD合并高血糖会加重肺限制性功能障碍及非弥散功能障碍, 增长住院时间, 增高患者死亡率。

关键词

间质性肺疾病, 空腹血糖, 肺功能

Study on the Relationship between Fasting Blood Glucose and Interstitial Lung Disease

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Abstract

Objective: To explore whether hyperglycemia is a risk factor for interstitial lung disease, and whether hyperglycemia leads to poor prognosis in patients with interstitial lung disease. **Methods:** The data of hospitalized patients from January 2019 to December 2019 in the Affiliated Hospital of Qingdao University were collected. Patients with interstitial lung disease were the experimental group (150 cases), and those without interstitial disease were the control group (300 cases). The difference in fasting blood glucose between patients of the two groups was compared; the patients with interstitial lung disease were divided into hyperglycemia group (51 cases) and normal blood glucose group (99 cases) according to fasting blood glucose, and prognostic indicators such as blood gas analysis, six-minute walking distance, lung function, length of stay, and mortality rates in the two groups were compared. **Results:** 1) The fasting blood glucose level in the interstitial lung disease group was significantly higher than that in the non-interstitial lung disease group ($p < 0.05$). 2) Compared with the normal blood glucose group (99 cases), the hyperglycemia group (51 cases) had lower oxygen partial pressure, carbon dioxide partial pressure, oxygen saturation, FVC, FEV1, DLCO, PEF, longer hospital stay, and higher mortality rates; the difference is statistically significant ($p < 0.05$); there is no statistically significant difference in age and BMI ($p > 0.05$). 3) Pearson correlation analysis results show that fasting blood glucose level is positively correlated with length of hospital stay ($r = 0.232, p < 0.05$), and negatively correlated with oxygen partial pressure ($r = -0.311, p < 0.05$), oxygen saturation ($r = -0.255, p < 0.05$), FVC ($r = -0.312, p < 0.05$), FEV1 ($r = -0.301, p < 0.05$), DLCO ($r = -0.222, p < 0.05$), PEF ($r = -0.627, p < 0.05$). **Conclusion:** Hyperglycemia can cause lung damage and is one of the independent risk factors for ILD. ILD combined with hyperglycemia can aggravate restrictive pulmonary dysfunction and non-diffuse dysfunction, increase hospital stay, and increase patient mortality.

Keywords

Interstitial Lung Disease, Fasting Blood Glucose, Pulmonary Function

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1. 引言

肺间质纤维化是由多种因素引起的以肺组织纤维化为主要病理表现的慢性进展性疾病，发病率高，死亡率高，给患者造成的经济负担重。肺纤维化至今尚无明确的病因，是多种疾病的共同表现和并发症。糖尿病患者后期多有心血管、肾脏、视网膜、神经系统等慢性并发症。近年来，许多研究发现，糖尿病患者的肺部也呈现出与心肌、肾脏等相类似的组织纤维样变化，这说明高血糖可能是肺纤维化发生的危险因素之一。

2. 资料与方法

2.1. 一般资料

收集青岛大学附属医院 2019 年 1 月~2019 年 12 月住院患者病例资料，间质性肺疾病者为实验组，无间质性肺疾病者为对照组。符合 2008 年英国胸科学会、澳大利和新西兰胸科学会及爱尔兰胸科协会联合

发布的《间质性肺病指南》[1]中ILD的诊断标准,并经高分辨率计算机断层扫描技术(HRCT)、实验室检查、病史等确诊。本研究经青岛大学附属医院医学伦理委员会审核批准,所有患者均知情同意。

2.2. 纳入/排除标准

间质性肺病组:1) 纳入年龄40~80岁之间患者;2) 排除使用激素治疗患者;3) 排除慢性阻塞性肺疾病、支气管哮喘等肺部疾病者。对照组:1) 纳入年龄40~80岁之间患者;2) 排除使用激素治疗患者;3) 排除慢性阻塞性肺疾病、支气管哮喘等肺部疾病者。

2.3. 按空腹血糖分组标准

参考《中国2型糖尿病防治指南(2017年版)》[2]糖尿病诊断标准:空腹血糖 ≥ 7.0 mmol/L和/或糖负荷后2h血糖 ≥ 11.1 mmol/L或糖化血红蛋白 $> 6.3\%$ 。

2.4. 分析指标

比较间质性肺疾病组和无间质性肺疾病组空腹血糖、年龄、BMI、性别比例是否存在差异;将间质性肺病患者按空腹血糖分为高血糖组和正常血糖组,分析两组患者血气分析、肺功能、住院时长、再住院率、死亡率等预后指标是否存在差异。

2.5. 统计学方法

应用SPSS 26.0统计学软件进行数据处理,计量资料以($\bar{x} \pm s$)表示,两组间比较采用两独立样本t检验;血糖与ILD患者血常规、CRP、血气分析、肺功能、住院时长的相关性分析采用皮尔逊相关分析。以 $p < 0.05$ 为差异有统计学意义。

3. 结果

3.1. 间质性肺疾病组与无间质性肺疾病组相关指标比较

间质性肺疾病组空腹血糖水平明显高于无间质性肺疾病组($p < 0.05$),两组间年龄、性别、BMI无统计学差异($p > 0.05$)(见表1)。

Table 1. Comparison of fasting blood glucose, age, BMI, and sex ratio between the two groups of patients

表 1. 两组患者空腹血糖、年龄、BMI、性别比例比较

组别	空腹血糖	年龄	BMI	性别(n)	
				男	女
ILD组	6.80 ± 2.71	64.18 ± 10.05	24.56 ± 3.76	86	64
对照组	5.47 ± 1.71	64.01 ± 10.73	24.01 ± 3.67	174	126
t(x ²)值	5.47	0.17	1.49	0.018 ^a	
p值	<0.001	0.86	0.14	0.89	

注: a 为 x² 值; ILD = 间质性肺病。

3.2. ILD患者高血糖组与正常血糖组相关指标比较

高血糖组与正常血糖组比较,氧分压、二氧化碳分压、氧饱和度、FVC、FEV1、DLCO、PEF、住院时长、死亡率,差异具有统计学意义($p < 0.05$);年龄、BMI、六分钟步行距离,差异无统计学意义($p > 0.05$)(见表2)。

Table 2. Comparison of prognostic indicators between hyperglycemia group and normoglycemia group in ILD patients
表 2. ILD 患者高血糖组与正常血糖组预后相关指标比较

指标	高血糖	正常血糖	t(X ²)值	p 值
年龄	64.88 ± 6.80	64.88 ± 6.80	-2.52	0.80
BMI	24.59 ± 3.67	24.54 ± 3.83	0.07	0.94
氧分压	70.52 ± 16.20	80.23 ± 18.92	-3.04	0.00
二氧化碳分压	38.52 ± 4.58	40.28 ± 3.58	-2.50	0.01
氧饱和度	93.5 ± 4.84	95.42 ± 4.18	-2.34	0.02
FVC	70.66 ± 23.45	82.62 ± 21.20	-2.41	0.02
FEV1	76.50 ± 24.75	88.60 ± 21.55	-2.37	0.02
DLCO	60.08 ± 23.75	93.39 ± 17.16	-6.58	0.00
PEF	90.37 ± 22.91	104.24 ± 26.89	-2.35	0.01
住院时长	15.90 ± 11.13	11.2 ± 7.19	2.76	0.00
死亡率	-	-	11.44 ^a	0.00

注: a 为 χ^2 值。

3.3. 皮尔逊相关性分析

皮尔逊相关分析结果显示, 空腹血糖水平与住院时长($r = 0.232, p < 0.05$)呈正相关, 与氧分压($r = -0.311, p < 0.05$)、氧饱和度($r = -0.255, p < 0.05$)、FVC ($r = -0.312, p < 0.05$)、FEV1 ($r = -0.301, p < 0.05$)、DLCO ($r = -0.222, p < 0.05$)、PEF ($r = -0.627, p < 0.05$)呈负相关。

4. 讨论

间质性肺疾病(Interstitial lung disease, ILD)是 200 多种不同疾病的总称[3], 是一组肺异质性疾病, 包括 200 多个以肺实质广泛纤维化和/或炎性异常为特征的肺实质病变[4], 具有相当高的发病率和死亡率[5]。肺间质纤维化至今尚无明确的病因, 是多种疾病的共同表现和并发症。

糖尿病(DM)不仅是一种常见的慢性病, 而且是一个全球性的健康问题。世界卫生组织(World Health Organization)报告称, 糖尿病患者的数量已从 1980 年的 1.08 亿人增加到 2014 年的 4.22 亿人, 占世界成年人口的 8.5% [6]。据国际糖尿病联合会估计, 到 2035 年, 全球糖尿病患者人数将上升到 5.92 亿人[7]。近几十年来, 全球糖尿病患病率一直在稳步上升, 至 2015 年, 20~79 岁成年人的糖尿病患病率为 8.8%, 预计 2040 年将增至 10.4% [8]。

黄敬等[9]于镜下观察 2 型糖尿病大鼠模型肺组织, 可见肺组织形态改变, 并有胶原沉积, 说明肺脏是糖尿病的靶器官, 并表现为纤维化。陈中明[10]等研究了高血糖对链脲佐菌素(STZ)诱导的糖尿病沙土鼠肺 EMT 的影响。与非糖尿病沙土鼠相比, 糖尿病沙土鼠的肺泡空隙体积分数显著降低, 肺间隔厚度、肺泡壁体积分数和肺损伤评分显著升高。这项研究表明, 在实验性糖尿病模型中, 高血糖诱导 EMT 并促进肺纤维化[10]。

德国的一项研究在一家门诊对 280 名参与者(年龄在 18 岁到 75 岁之间)进行了筛查, 以调查糖尿病前期和 2 型糖尿病患者限制性肺部疾病和 ILD 的发生率[11]。对 5 名患有 2 型糖尿病、呼吸困难和限制性肺部疾病的受试者进行了高分辨率计算机断层扫描(CT)和 6 min 步行试验。在 5 名患者中, 有 4 名患者被诊断为 ILD, 组织学分析显示 ILD 纤维化[11]。这项研究显示, 2 型糖尿病患者呼吸困难和 ILD 的风险增加[11]。

糖尿病是一种全身性疾病,以慢性高血糖状态为特征,与炎症和氧化应激有关。这会导致许多器官的微血管和大血管损伤,特别是肾脏、视网膜和心血管系统[12][13][14][15],使这些至关重要的器官丧失功能,并导致死亡[16][17][18][19]。糖尿病对这些器官的微血管和大血管损害的临床基础和分子机制已被广泛研究。肺由丰富的肺泡-毛细血管网和结缔组织组成,提示它可能是糖尿病微血管损害的靶点。不幸的是,这种相关性常常被忽视,缺乏将肺当作糖尿病损害靶点的研究和证据[20][21][22]。高血糖已被证实可导致间质纤维化和肺泡毛细血管微血管病变[23],它与限制性和阻塞性肺功能损害有关,包括1秒用力呼气量(FEV1)、用力肺活量(FVC)、肺弥散能力(DLCO)和肺弹性回缩[24][25]。它还被证明会导致气道粘液的过度产生,导致许多肺部疾病的发病率和死亡率[26]。

5. 结论

综上所述,高血糖可致使肺部受损,是导致ILD的独立危险因素之一。肺间质纤维化主要病理变化表现在微血管的改变和胶原蛋白积聚,这与高血糖导致的微血管病变密不可分。ILD合并高血糖会加重肺限制性功能障碍及非弥散功能障碍,增长住院时间,增高患者死亡率。因此及早发现、筛查和提高对糖尿病相关间质性肺疾病的认识,控制糖尿病患者血糖,以期降低高血糖所致的间质性肺疾病。但该研究存在一定的局限性,例如:病例数少,部分间质性肺疾病合并其他疾病(可能会对血糖有一定影响)等,未来仍需更多临床数据及相关的实验研究来进一步证实本研究的精确性。

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