

糖尿病患者COVID-19感染后的心理状态变化及其影响因素

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摘 要

糖尿病与许多神经精神疾病有关, 尤其是焦虑、抑郁。众所周知, 糖尿病患者的抑郁症发生率是普通人群的2~3倍。糖尿病症状、并发症、疾病负担加重、自我护理不足、残疾和生活质量下降在共病抑郁和/或焦虑患者中更常见。压力是糖尿病患者的主要危险因素, 它使血糖控制恶化, 从而导致更多的症状和并发症。全球COVID-19爆发对大多数人来说都是一次压力很大的经历, 糖尿病患者特别容易受到COVID-19不良后果的影响。研究表明, COVID-19大流行对糖尿病等慢性病患者的心理影响大于非慢性病患者。COVID-19后糖尿病患者心理状况会产生变化, 糖尿病患者COVID-19感染后的心理状态的变化及其影响因素极其复杂, 本文旨在分析糖尿病患者COVID-19感染后心理状态的变化及其影响因素, 并对糖尿病患者存在焦虑抑郁患者的心理干预及整体治疗提供指导。

关键词

糖尿病, COVID-19, 心理状况

Changes in Psychological Status of Diabetic Patients after COVID-19 Infection and Its Influencing Factors

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Abstract

Diabetes is associated with many neuropsychiatric disorders, especially anxiety and depression. Depression is known to be 2~3 times more common in people with diabetes than in the general population. Diabetic symptoms, complications, increased disease burden, inadequate self-care, disability, and decreased quality of life are more common in patients with co-morbid depression and/or anxiety. Stress is a major risk factor for people with diabetes and worsens glycaemic control, leading to more symptoms and complications. A global COVID-19 outbreak is a stressful experience for most people, and people with diabetes are particularly vulnerable to the adverse consequences of COVID-19. Studies have shown that the psychological impact of the COVID-19 pandemic on patients with chronic diseases such as diabetes mellitus is greater than that of patients with non-chronic diseases. Changes in the psychological status of diabetic patients occur after COVID-19. Changes in the psychological state of diabetic patients after COVID-19 infection and the factors influencing them and their complexity are discussed in this paper. The purpose of this paper is to analyse the changes in the psychological state of diabetic patients after COVID-19 infection and its influencing factors, and to provide guidance for psychological intervention and overall treatment of diabetic patients with anxiety and depression

Keywords

Diabetes Mellitus, COVID-19, Psychological Condition

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1. 糖尿病、抑郁、焦虑流行病学

糖尿病是一种以碳水化合物、蛋白质和脂肪代谢紊乱引起血糖异常的慢性疾病[1]。糖尿病的特征是慢性、低度炎症、受损血糖控制、内皮功能障碍、高凝状态和进展缓慢微血管和大血管形式的多组织损伤并发症[2] [3]。在全球范围内,焦虑和抑郁是最常见的精神疾病,给个人和社会增加了很大的负担。焦虑障碍的定义是一种以广泛和持续性焦虑或反复发作的惊恐不安为主要特征,常伴有自主神经紊乱、肌肉紧张与运动性不安等神经症,病程标准为6个月。焦虑在人们的生活中普遍存在,表现为显著的负性情绪、紧张的躯体反应,对发生或未发生的事件产生紧张、不安、忧虑、烦恼等复杂情绪,甚至合并睡眠障碍[4]。抑郁症是一种广泛存在的慢性心理疾病,属于情绪障碍,会导致持续的悲伤感和兴趣丧失,有抑郁症的共同特征是悲伤,空虚或烦躁的情绪,伴随着躯体和认知变化,显著影响个体的功能能力。抑郁障碍是全球精神障碍所致疾病负担的首要原因,已成为全球重大公共卫生问题[5]。焦虑症很少单独发生,经常与抑郁或其他心理健康问题同时出现。

2. 糖尿病患者新冠病毒感染后抑郁、焦虑患病率

许多研究探讨了糖尿病患者感染新冠病毒后抑郁、焦虑的患病率。一项荟萃分析研究发现,在2型糖尿病(T2DM)患者中,焦虑和抑郁的患病率分别为20%和36% [6]。某试验的专门中心对2523例糖尿病患者(1427例T1D、1037例T2D、59例其他类型)进行筛查[7],确定了1154例抑郁症状升高(T1D: 44.6%, T2D: 46.6%)。一项评价[8]确定了33篇文章,共涉及50,905名慢性病患者。进行了四项meta分析来估

计抑郁症的患病率。在糖尿病患者中, 患病率从 17%到 33%不等。在大流行之前, 2 型糖尿病患者的抑郁患病率为 10.6%~17% [9] [10]。这些数据提供了证据, 表明抑郁症状的患病率在大流行期间有所增加[11]。不同国家间的焦虑、抑郁的患病率有所不同, 这可能与社会支持、医疗水平、教育、文化、收入等相关, 在低收入和中等收入国家, T2DM 患者的抑郁症患病率估计在 25%至 45%之间, 平均为 35.7%。这些估计值明显高于高收入国家的估计值, 高收入国家的合并症抑郁症患病率为 25% [12]。

3. 糖尿病患者新冠病毒感染后焦虑抑郁的发病机制

首先需探讨糖尿病和焦虑、抑郁共同可能的发病机制, 糖尿病和焦虑、抑郁之间存在双向关联。许多机制被认为与焦虑抑郁和糖尿病之间的联系有关, 包括: HPA 轴功能失调、炎症、昼夜节律紊乱、神经生物学因素、胰岛素抵抗等[13]。HPA 轴功能失调: 糖尿病患者病程长、低血糖事件更频繁及血糖和并发症控制不佳均可增加患者的压力, 导致 HPA 轴的失衡, 海马中存在丰富的糖皮质激素受体, 长期血浆高皮质醇可作用于该受体, 导致神经发生和突触可塑性减低及海马细胞凋亡[14], 导致情绪改变。早期应激可减慢海马发育, 2 型糖尿病和抑郁症中都存在的海马体积减小, 可能是两者的共同病理生理机制引发焦虑和抑郁[15]。炎症反应: 在患焦虑和抑郁的糖尿病患者中, 可溶性环氧化物水解酶的衍生物浓度相对较高, 可溶性环氧化物水解酶可催化环氧化物水解, 使其失去强抗炎和保护神经元的作用, 并产生缺乏这些功能的二醇[16]。二醇这种代谢产物具有细胞毒性, 能干扰神经元的正常功能, 导致神经元死亡[16]。慢性应激直接或间接经 HPA 轴激活炎症系统, 导致 IL-6、TNF- α 、INF- γ 等促炎细胞因子水平升高。IL-6、C 反应蛋白等炎症因子可能是抑郁与高血糖等代谢综合征的共同病理机制[17]。促炎细胞因子可以通过氧化应激导致脑源性神经营养因子下降, 或增加色氨酸的降解导致 5-羟色胺水平减低, 从而导致抑郁症[18]。总之, 炎症反应不仅增加焦虑和抑郁的风险, 而且还通过不同途径影响神经元正常功能。胰岛素抵抗: 2 型糖尿病患者中胰岛素抵抗患病率超过 80%, 胰岛素抵抗可表现为中枢胰岛素抵抗和外周胰岛素抵抗。中枢胰岛素抵抗表现为调节代谢能力障碍, 可能引发线粒体和多巴胺系统功能紊乱, 可导致认知和情绪功能受损[19]。有研究显示, 胰岛素抵抗水平高的青年前扣带回和海马体积缩小与抑郁症状呈负相关关系[20]。小鼠下丘脑中胰岛素受体敲除会引发抑郁焦虑样行为[20], 提示中枢胰岛素抵抗与认知情感功能障碍相关。下丘脑弓状核胰岛素受体的敲除可导致加压素对束缚应激的反应降低, 表明中枢胰岛素抵抗可能引起 HPA 轴功能紊乱[21] [22], 而 HPA 轴紊乱与 2 型糖尿病及抑郁症发生均相关。

而 COVID-19 后焦虑抑郁症状的精神病理学机制主要与对病毒感染的外周免疫炎症反应引发的炎症、通过中枢神经系统(CNS)的直接病毒感染、通过免疫反应间接诱发精神病理学后遗症以及感染期间和感染后的持续心理负担相关[23] [24]。以下将对其可能机制进行阐述: 其一, 感染后会诱导免疫炎症反应, 炎症过程导致的免疫失调被广泛地与心境障碍有关[25] [26]。COVID-19 患者在重度和非重度感染中都表现出相同的分子炎症途径, 这表明抑郁症和 COVID-19 感染之间存在先天免疫激活和促炎标志物增加的共同结果。TNF α 、IL-1 β 和 IL-6 等外周炎症标志物通过影响内皮细胞来增加血脑屏障的通透性[27]。反过来, 减弱的血脑屏障可能促进微生物和其他炎症介质进入大脑。一旦进入大脑, 细胞因子可引起脑神经回路和神经发生的多种变化, 损害边缘系统区域的功能, 从而导致抑郁症状[28]。这些变化与不同的机制有关, 包括影响神经传递、小胶质细胞、氧化应激和 HPA 的改变[29] [30]。其中神经递质代谢的变化与抑郁精神病理学广泛相关[31], 受炎症影响较大的神经递质是血清素、多巴胺和谷氨酸, 它们的合成、释放和再摄取会发生变化。此外, 当炎症到达大脑时, 它可以改变小胶质细胞和星形胶质细胞的活性, 而小胶质细胞活化与 COVID-19 的急性和慢性神经系统并发症有关[32], 有趣的是, HPA 轴和免疫系统之间存在双向关系。细胞因子可以通过最终增加糖皮质激素通过肾上腺皮质的释放来促进 HPA 轴的激活

[33]。在促炎细胞因子的作用下, 内皮细胞和小胶质细胞合成前列腺素 E2 (PGE2), 前列腺素 E2 作用于下丘脑分泌促肾上腺皮质激素释放因子的神经元, 从而促进糖皮质激素的合成和释放。除了这些机制外, 在 COVID-19 中, 下丘脑 ACE2 水平的下调被认为是冠状病毒诱导 HPA 轴过度活跃的潜在机制[33]。在生理条件下, 细胞因子有助于神经发生、突触缩放和重塑以及长期增强, 从而在学习和记忆中发挥核心作用[34] [35]。在外周和中枢炎症中, 大脑细胞因子水平升高, 突触可塑性、学习和记忆受到抑制[36], 这也是因为促炎细胞因子减少了脑源性神经营养因子, 促炎细胞因子负责结构和功能细胞支持。这些变化在抑郁症中被广泛报道, 并被认为是该疾病中观察到的行为和心境改变的基础[37]。其二, 除了 COVID-19 感染的直接影响外, 重要的心理压力源可能在 COVID-19 患者精神病理学结果的发展中发挥重要作用。对未来的不确定性以及感染患者经历的幸存者内疚感可能诱发感染后的抑郁症状[38] [39]。心理应激会激活 HPA 轴和交感神经系统(sympathetic nervous system, SNS), 特别是与焦虑和抑郁等心理健康状况相关[40]。持续的心理压力会诱发激素水平的变化以及神经元和 HPA 对糖皮质激素的反应[41] [42], 从而通过中枢神经系统的免疫调节来影响情绪[43]。

在 COVID-19 的环境下, 糖尿病与精神健康障碍之间的关联可能会加剧, 心理困扰可能会增加焦虑抑郁症状并导致不良的糖尿病结局[44] [45]。糖尿病患者新冠病毒感染后焦虑抑郁患病率升高的机制鲜有相关文献, 综上分析, 可能为以下机制: 糖尿病与焦虑抑郁的共同发病机制以及新冠病毒感染后所致焦虑抑郁的发病机制中存在共同点为炎症反应、HPA 轴功能失衡, 糖尿病发生的病理变化非常类似于 COVID-19 感染中发生的急性变化, 但具有更多长期或慢性病程。COVID-19 中释放的许多促炎分子细胞因子风暴, 例如 C 反应蛋白(CRP)和白细胞介素 6 (IL-6), 是与糖尿病相关的炎症过程产生的那些相同, 这可能助长细胞因子释放和广泛的多器官损伤的恶性循环, 特别是在已经受糖尿病影响的组织中[46]。急性 COVID-19 可能会放大预先存在的炎症[47]。通过氧化应激导致脑源性神经营养因子下降, 或增加色氨酸的降解导致 5-羟色胺水平减低以及通过不同途径影响神经元正常功能, 从而导致焦虑、抑郁[18]。COVID-19 大流行对大多数人来说都是一次压力很大的经历, 糖尿病患者害怕受到病毒的过度影响、将糖尿病患者标记为高危人群的耻辱感、预后较差以及感染后血糖控制差等因素, 对于糖尿病患者来说压力更大, 导致 HPA 轴的失衡, 海马中存在丰富的糖皮质激素受体, 长期血浆高皮质醇可作用于该受体, 导致神经发生和突触可塑性减低及海马细胞凋亡[15], 导致焦虑、抑郁。

4. 糖尿病患者新冠病毒感染后焦虑、抑郁的影响因素

据报道, 在 COVID-19 大流行期间, 与糖尿病患者出现焦虑抑郁症状相关的因素包括: 女性[48], 单身, 缺乏宗教信仰, 受教育程度较低, 吸烟, 有焦虑和/或抑郁史, 收入较低和兼职工作或远程学习。与年龄有关, 一些作者指出年龄较小是一个诱发因素, 而另一些研究者则认为没有显著相关性。糖尿病患者焦虑抑郁水平升高相关的临床参数包括 HbA1c 升高、每日血糖时间范围降低、长期糖尿病和睡眠障碍[9] [49] [50]。另一项研究[51]发现 COVID-19 流行期间与糖尿病患者焦虑抑郁相关的因素为男性、年龄较大、居住在城市地区、教育水平较低、从事体力劳动、失业、收入低、吸烟、饮食品种较少或不进行中度至剧烈运动的患者患抑郁症或焦虑症的风险增加。

5. 小结

COVID-19 大流行给糖尿病患者带来了新的挑战, 除了慢性病的需求和管理带来先前存在的挑战外, 还导致他们经历高水平的心理健康问题, COVID-19 大流行加重了糖尿病患者的焦虑抑郁水平, 这凸显了早期心理干预的必要性, 对他们进行心理评估是非常有必要的, 以满足其心理健康需求, 以及对糖尿病血糖的控制及并发症的管理提供帮助。

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