

经皮冠状动脉介入治疗术后新发焦虑抑郁 机制的研究进展

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[摘要] 经皮冠状动脉介入治疗(PCI)现已成为临床广泛应用的心血管疾病治疗策略。PCI术作为一种有创治疗手段,患者在术后易发生焦虑抑郁的负面情绪,严重影响预后。近年来,随着双心疾病的研究发展,医师愈加关注重视心理因素对心脏疾病的影响。西医认为PCI术后发生焦虑抑郁主要与炎症反应、血小板聚集、神经内分泌机制以及D型人格学说有关,并基于此给予患者药物治疗及非药物治疗。本文主要对PCI术后引发焦虑抑郁的发病机制进行综述。

[关键词] 经皮冠状动脉介入治疗; 焦虑; 抑郁; 发病机制; 中西医治疗

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Research progress on the mechanism of new anxiety and depression after percutaneous coronary intervention

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[Abstract] Percutaneous coronary intervention (PCI) has become a widely used strategy for the treatment of cardiovascular disease. As an invasive treatment, patients are susceptible to anxiety and depression in the postoperative period, which seriously affects their prognosis. In recent years, with the development of research on double heart disease, physicians have become more concerned about emphasizing the impact of psychological factors on heart disease. Western medicine believes that anxiety and depression after PCI is mainly related to inflammatory response, platelet aggregation, neuroendocrine mechanism and D-type personality theory, and based on this, patients are given pharmacological and non-pharmacological treatments. This article mainly reviews the pathogenesis of anxiety and depression after PCI.

[Key words] Percutaneous coronary intervention; Anxiety; Depression; Pathogenesis; Traditional Chinese and Western medicine treatment

经皮冠状动脉介入治疗(percutaneous coronary intervention, PCI)术是通过心导管技术疏通狭窄甚至闭塞的冠状动脉管腔以改善心肌血流灌注的治疗方法。PCI术可快速有效地使冠状动脉粥样硬化性心脏病(冠心病)患者狭窄的冠状动脉复通,在急性冠脉综合征的治疗中具有举足轻重的地位。PCI比传统溶栓药物治疗更具有优势,但作为一种有创治疗手段,在术前、术中或术后会给患者造成较大的心理压力,同时在术后患者会产生不适症状,甚至发生

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重大不良心血管事件(major adverse cardiovascular events, MACE)等加剧患者的负面情绪,负面情绪的积压极可能触发恶性循环,使患者身体的应激反应加剧,进一步影响心脏功能恢复,降低治疗效果及预后。焦虑抑郁是术后负面情绪的主要表现。我国尚缺少全国性的关于PCI术后患者的焦虑抑郁发病率的调查统计,仅有各个地区医院散在的分布调查,青岛大学附属医院^[1]针对中青年PCI术后焦虑抑郁发病检出率为37.4%~67.5%,首都医科大学附属北京安贞医院^[2]的检出率为1.4%~37.6%,了解PCI术后发生焦虑抑郁的机制是确定治疗方案的前提。本文对PCI术后发生焦虑抑郁心理障碍的病理机制

研究进展做一综述。

1 焦虑抑郁与炎症反应机制

在 PCI 过程中,无论是采取药物涂层球囊扩张技术,还是选用药物洗脱支架植入手段,均需医护人员在冠状动脉这一极为精细的管道内进行扩张与放置操作。由于冠状动脉管壁本身的脆弱性以及操作的侵入性,机械损伤在所难免。损伤必然会导致局部的炎症反应且会激活血小板凝血系统^[3-4]。炎症反应是被普遍认可的用来解释 PCI 术后引发焦虑抑郁的假设机制。焦虑抑郁是动脉粥样硬化和冠心病发展的已知危险因素。发生急性冠脉综合征后心肌细胞坏死以及行 PCI 术后,短暂的缺血与血液的再灌注损伤都会通过诱导氧化应激触发促炎性细胞因子释放并参与炎症反应^[5]。焦虑抑郁的发生与持续的炎症状态和炎症细胞因子浓度的增加有关,包括 C 反应蛋白(C-reactive protein, CRP)和各种细胞因子,如肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)、白细胞介素(interleukin, IL)-1 β 、IL-6、IL-10 和 IL-17 等^[6-7],这些炎症细胞因子能够改变细胞内代谢过程,以促进氧化应激和神经凋亡,进而引起焦虑和抑郁。既往的研究发现^[8-9],与非冠心病患者相比,冠心病患者的促炎性细胞因子 TNF- α 、IL-17 升高,表明炎症细胞因子可能引起血管内皮损伤、促进动脉粥样硬化等,进而增加 MACE 的发生风险^[10-11]。相反地,研究表明,抑郁症状会影响未来的 CRP 水平^[12],CRP 水平的升高与后续焦虑抑郁的发作关系甚微^[13],故提出是焦虑抑郁导致炎症状态,而不是炎症状态导致焦虑抑郁。焦虑抑郁会激发交感神经的兴奋,从而影响炎症细胞因子的释放,加重炎症反应^[14],CRP 水平升高与抑郁症之间呈正相关^[15],故有学者支持通过炎症预测焦虑抑郁。

2 焦虑抑郁与血小板聚集机制

PCI 会激活血小板系统,血小板活化增加、血栓形成是焦虑抑郁和冠心病之间关联的另一种病理机制^[16]。焦虑抑郁与脑源性神经营养因子(brain-derived neurotrophic factor, BDNF)和 5-羟色胺(5-hydroxytryptamine, 5-HT)的缺乏密切相关^[17],且二者对血小板(platelet, PLT)的激活与焦虑抑郁的产生往往是平行的。BDNF 最早被发现在大脑中,而大部分的 BDNF 则主要储存于外周循环 PLT 内,当 PLT 被激活发生凝血过程时可将其释放到血液循环中,促进神经细胞、血管内皮细胞等存活和修复,发挥调节情绪、保护心脏的作用^[18-19],PLT 被激活时,纤溶酶原激活剂抑制剂-1(plasminogen activator inhibitor-1, PAI-1)会在血栓形成部位释放,以防

止动脉粥样硬化斑块中的血凝块溶解,PAI-1 的相对含量决定对溶栓的抵抗力。血栓的增加会造成 PAI-1 水平升高,从而抑制 BDNF 的转化生成^[20],从而引起情绪异常,并进入恶性循环中,最终增加心血管事件的发生风险。5-HT 是由色氨酸(tryptophan, Trp)衍生的中枢神经递质,Trp 通过色氨酸羟化酶(tryptophan hydroxylase, TPH)合成 5-羟色氨酸(5-hydroxytryptophan, 5-HTP),然后 5-HTP 通过 5-羟色氨酸脱羧酶(5-hydroxytryptophan decarboxylase, 5-HTPDC)产生 5-HT。5-HTP 可以有效地增强中枢神经系统 5-HT 的合成,提高 5-HT 水平以发挥抗抑郁功能^[21]。PLT 细胞膜上含有 5-HT 受体,PLT 是体内 5-HT 主要转运载体和储存场所。5-HT 通过 5-HT 转运体进入 PLT 内,活化 PLT,诱导血小板聚集,并促进血管平滑肌细胞的收缩,多种通路共同作用,促进血栓形成,加速动脉粥样硬化^[22],血清中的 5-HT 水平降低,抗抑郁功能减弱,进而使患者处于抑郁状态。

3 焦虑抑郁与神经内分泌机制

自主神经系统(autonomic nervous system, ANS)分为交感神经和副交感神经系统,交感神经系统和副交感神经系统之间的不平衡,被认为是焦虑抑郁与不良心血管预后之间的关键机制。心率变异性(heart rate variability, HRV)可能是评估人类心脏自主功能使用最广泛的方法^[23]。它能反映心脏对环境 and 外部刺激时的自主反应,评估自主神经功能,量化心脏交感和副交感的神经控制功能^[24]。与没有抑郁症的人群相比,抑郁患者的 HRV 较低,较低的 HRV 是 MACE 的风险因素^[25],HRV 与心脏迷走神经控制不良的联系在抑郁症男性中更强,该联系表现出了明显的性别差异。焦虑抑郁使交感神经系统兴奋,下丘脑-垂体-肾上腺(hypothalamic-pituitary-adrenal, HPA)轴过度激活,抑制 γ -氨基丁酸(γ -aminobutyric acid, GABA)的释放,GABA 对自主神经系统产生的抑制性调控降低,交感肾上腺髓质功能亢进,促进促肾上腺皮质激素(adrenocorticotrophic hormone, ACTH)的分泌^[26],打破了交感神经和副交感神经的平衡性,影响心脏的节律性,进而造成显著的 HRV 变化;与此同时,ACTH 会刺激肾上腺释放皮质醇,导致皮质醇水平上升及皮质醇节律异常^[27],糖皮质激素水平的慢性增加会阻碍胰岛素促进细胞吸收葡萄糖的能力,使体内糖脂代谢紊乱,产生胰岛素抵抗,诱发机体的慢性炎症反应,从而使血液黏稠,促进动脉粥样硬化,增加冠心病的发生风险^[28]。

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