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【综述】

吸烟诱发心血管疾病研究进展

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摘要: 吸烟是心血管疾病的主要可预防危险因素之一。烟草中许多化学成分对心血管系统有害,目前已知的成分主要有尼古丁、一氧化氮、亚硝胺、多环芳香烃、氢氰化物和醛类等。吸烟容易使个体出现动脉粥样硬化综合征,包括稳定型心绞痛、急性冠状动脉综合征、卒中以及主动脉和周围动脉粥样硬化,严重影响人们的健康。本文就吸烟对心血管疾病的影响及机制进行综述。

关键词: 吸烟;动脉粥样硬化综合征;心血管疾病

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Research progress on smoking induced cardiovascular diseases

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Abstract: Smoking is one of the main preventable risk factors for cardiovascular disease. Many substances in tobacco are harmful to the cardiovascular system, and currently known components mainly include nicotine, nitric oxide, nitrosamines, polycyclic aromatic hydrocarbons, hydrocyanides, and aldehydes. Smoking is easy to cause atherosclerosis syndrome in individuals, including stable angina pectoris, acute coronary syndrome, stroke, and aorta and surrounding atherosclerosis, which seriously affects the health of people. This article reviews the effect and mechanism of smoking on cardiovascular disease.

Key words: smoking; atherosclerosis syndrome; cardiovascular disease

吸烟是导致心血管疾病 (cardiovascular diseases, CVD) 的主要可预防危险因素之一^[1]。CVD 是指与包括心脏和血管在内的血液循环系统相关的疾病。常见的 CVD 包括缺血性心脏病、外周动脉疾病、心律失常、高血压、心力衰竭、心脏瓣膜病等。烟草中含有多种对心血管系统有害的化学成分,目前已知的成分中主要包括尼古丁、一氧化碳、亚硝胺、多环芳香烃、氢氰化物、醛类和重金属等^[1]。此外,流行病学和临床研究表明,吸烟量的增加和时间的延长可增加心血管事件的发生风险^[2-5]。吸烟与心血管系统疾病关系密切,吸烟可对炎症和免疫反应、血脂、血压产生影响,并可导致心律失常、心力衰竭、

心脏瓣膜病等常见心血管疾病的发生。本文就吸烟对 CVD 的影响及机制进行综述。

1 吸烟诱发 CVD 的机制

1.1 吸烟对炎症和免疫反应的影响

LUETRA-GOON 等^[6]在吸烟者中发现了免疫抑制和炎症反应情况。吸烟会导致呼吸道上皮细胞大量死亡,坏死细胞诱导的促炎信号释放到周围的微环境和血液循环,触发一系列信号级联反应,使炎症细胞产生促炎介质,如细胞因子、趋化因子和 C 反应蛋白等,最终导致炎症反应^[7]。有研究表明,与非吸烟者比较,吸烟者外周血中中性粒细胞、单核细胞、淋巴细胞、嗜碱性粒细胞、超敏 C 反应蛋白、单核细胞趋化蛋白-1 (monocyte chemotactic protein-1, MCP-1)、 γ -干扰素 (interferon- γ , IFN- γ) 水平较高,表明吸烟会引起炎症和免疫反应^[8]。

1.1.1 MCP-1 有研究发现,随着吸烟时间的延长,吸烟者体内 MCP-1 水平逐渐升高^[9]。MCP-1 又

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称单核细胞趋化和激活因子(monocyte chemotactic and activating factor, MCAF),属于 C-C 亚族(β 亚族)成员,主要由单核细胞、巨噬细胞和血管内皮细胞分泌产生。MCP-1 可与单核细胞表面 MCP-1 受体发生特异性结合,从而诱导单核细胞迁移到血管壁炎症部位^[10]。单核细胞通过内皮细胞层迁移后分化为巨噬细胞,巨噬细胞可通过吸收低密度脂蛋白(low density lipoprotein, LDL)和氧化型低密度脂蛋白(oxidized low density lipoprotein, ox-LDL)形成富含胆固醇的泡沫细胞和早期脂质条纹,然后通过平滑肌细胞的增殖逐渐发展为复杂病变^[11-16]。活化的内皮细胞和泡沫细胞持续释放 MCP-1,使炎症和脂质持续积累^[17]。同时,MCP-1 在内皮细胞功能失调和粥样斑块的不稳定及破裂中发挥重要作用^[18]。

1.1.2 IFN- γ 吸烟使个体容易发生动脉粥样硬化综合征,包括稳定型心绞痛、急性冠状动脉综合征、卒中以及主动脉和周围动脉粥样硬化,导致间歇性跛行和腹主动脉瘤^[19-20]。动脉粥样硬化是引起心脑血管疾病的主要原因之一。吸烟加速动脉粥样硬化是相关心血管损害的主要途径。FROSTEGARD 等^[21]研究发现,与非吸烟者相比,发生动脉粥样硬化的吸烟者血浆 IFN- γ 水平升高。IFN- γ 是水溶性二聚体细胞因子,由活化 T 淋巴细胞、自然杀伤细胞、自然杀伤 T 淋巴细胞和抗原递呈细胞如巨噬细胞、树突细胞和淋巴细胞产生,具有抗病毒、免疫调节及抗肿瘤特性。IFN- γ 是免疫功能的关键调节因子,在动脉粥样硬化病变中高度表达,是动脉粥样硬化形成的重要因素^[22]。IFN- γ 同时具有促动脉粥样硬化和抗动脉粥样硬化作用,这可能是由于 IFN- γ 与动脉粥样硬化相关的多个信号通路有关^[22]。

1.1.3 微 RNA (microRNA, miRNA) miRNA 是一类内源性非编码小 RNA,在表观遗传水平上参与基因表达,可调节免疫相关细胞因子水平,对先天性和适应性免疫反应均有影响^[23-24]。miR-21 是促炎反应的关键调控因子,在许多疾病中表达上调,如心脏损伤、多发性肿瘤和炎症^[25]。miRNAs 对分子通路的调控较为复杂,与 CVD 的发展过程密切相关^[26]。然而,目前关于 miRNAs 在吸烟者动脉粥样硬化发生机制中的作用研究较少。

1.2 吸烟对血脂的影响 炎症可以改变高密度脂蛋白(high density lipoprotein, HDL)的组成、抗炎特

性和血清淀粉样蛋白 A 富集^[27-28]。高密度脂蛋白胆固醇(high density lipoprotein-cholesterol, HDL-C)水平与心血管事件风险呈负相关,而 ox-LDL 是动脉粥样硬化形成的重要因素之一。HDL 具有抗动脉粥样硬化的作用,除具有反胆固醇转运(reverse cholesterol transport, RCT)促进作用外,还能抑制 LDL 氧化、平滑肌细胞迁移和血小板聚集,改善内皮细胞功能障碍。SHEN 等^[29]研究表明,急性吸烟会削弱非吸烟者 HDL 的抗氧化能力。CHEN 等^[30]研究发现,与健康非吸烟者比较,冠状动脉性心脏病吸烟者和健康吸烟者的血浆 HDL 水平和 HDL 诱导的抗氧化、抗趋化能力显著降低;但在戒烟 3 个月后,冠状动脉性心脏病吸烟者体内 HDL 的抗氧化能力和抗趋化能力均显著提高,然而,HDL 诱导的细胞胆固醇外排并不因戒烟而增加。以上研究表明,吸烟可导致血脂异常,进而引起心血管疾病。

1.3 吸烟对血压的影响 目前,吸烟和高血压之间的直接因果关系尚不明确^[31-33]。OHTA 等^[34]研究表明,吸烟可增加高血压患者的血压和心率,这与副交感神经活动的减弱有关。相反,有流行病学研究发现,与不吸烟者相比,慢性吸烟者的血压较低^[35]。一项横断面研究发现,吸烟的老年男性的收缩压高于不吸烟者^[36]。另有研究表明,戒烟并不会降低血压,相反,其可能导致血压升高^[36]。ZHAGN 等^[37]研究发现,吸烟与夜间隐匿性高血压的发生率增加有关,尤其是在重度吸烟者或老年男性吸烟者中。有研究显示,吸烟可使自发交感神经活动增强,产生的增压反应可能促成高血压发生^[38]。总之,现有的数据尚不能证明吸烟习惯与血压值或持续高血压风险的关系,且长期戒烟后未观察到血压值降低。但有研究显示,高血压吸烟者更容易发展为更严重的高血压,包括恶性高血压和肾血管性高血压,这可能会加速动脉粥样硬化^[33],且更容易使动脉粥样硬化病变部位发生斑块破裂^[39]。

2 吸烟与常见 CVD

2.1 吸烟与心律失常 吸烟时释放到血液循环中的尼古丁会增加血浆儿茶酚胺浓度,且随着心肌工作和氧气需求的增加可能会导致心律失常的产生。烟草中的尼古丁可通过延长动作电位和膜去极化作用引起心律失常。此外,香烟中的一氧化碳也可导致心律失常。有研究发现,吸烟与青少年室性心律失常的发生有关^[40]。此外,ZUO 等^[41]研究表明,与

既往吸烟者(调查时已戒烟)比较,当前吸烟者发生心房颤动的风险较高。

2.2 吸烟与心力衰竭 心力衰竭是心血管疾病发展的终末阶段,是指心脏的舒张或收缩功能发生障碍。吸烟是心力衰竭的主要危险因素之一。碎裂QRS波(fragmented QRS complex,fQRS)是一个容易评估的非侵入性心电图参数,fQRS波的发生与心肌纤维化或心肌瘢痕引起的心肌活动改变有关,可预测心血管不良事件的发生^[42-43]。有研究通过检测fQRS发现,与不吸烟者相比,健康吸烟者左心室心肌收缩和舒张功能障碍的发生率增加,且左心室功能障碍与吸烟时间和强度有关^[42-43]。吸烟对心肌细胞有直接毒性作用^[44]。吸烟导致的长期炎症、内皮功能受损、心脏后负荷增加、肾功能恶化等会改变心肌的结构和功能,增加心房颤动的发生风险^[45]。另有研究表明,吸烟与射血分数降低型心力衰竭和射血分数保留型心力衰竭的发生有关^[46]。

2.3 吸烟与心脏瓣膜病 目前,关于吸烟对心脏瓣膜病影响的研究较少。吸烟可损伤主动脉瓣小叶,其机制可能为:烟草中的多种氧化性化学物质和自由基可改变脂蛋白组成,诱发促炎状态,促进血小板活化,从而促进膜间质细胞发生表型转化(从成纤维细胞变为成骨细胞),骨基质形成,进而导致狭窄程度加重^[47]。有研究表明,吸烟与退行性主动脉瓣疾病密切相关,且呈剂量依赖性^[48]。

3 小结

总之,吸烟与CVD密切相关。香烟烟雾可能改变正常细胞的表型和基因表达谱,诱导大量细胞死亡,从而可能触发局部或全身炎症反应,导致内皮细胞活化,脂质、脂蛋白和免疫细胞在血管壁沉积,促进血栓前阶段和动脉粥样硬化斑块形成,并随着时间的积累可导致冠状动脉不同程度的狭窄,从而导致CVD的发生。戒烟可降低CVD的发生风险,临床医生应积极劝阻吸烟。

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