

有关痛风、载脂蛋白B以及心血管疾病的 研究进展

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收稿日期: 2021年8月22日; 录用日期: 2021年9月12日; 发布日期: 2021年9月24日

摘 要

痛风是内分泌常见的代谢紊乱性疾病之一, 近些年来痛风的患病率逐年增加, 而且易合并脂蛋白代谢异常, 增加了痛风患者罹患心脑血管疾病的风险, 不利于痛风患者的生活质量; 同时脂蛋白代谢异常也是痛风发作及罹患心脑血管疾病的危险因素, 三者之间相互关联。近来研究发现, 痛风患者可伴有载脂蛋白B的异常, 其在心血管疾病风险预测的作用优于低密度脂蛋白。现通过对文献收集整理, 对痛风、载脂蛋白B以及心血管疾病的关

关键词

痛风, 载脂蛋白B, 心血管疾病, 动脉粥样硬化

Research Progress on Gout, Apolipoprotein B and Cardiovascular Diseases

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Received: Aug. 22nd, 2021; accepted: Sep. 12th, 2021; published: Sep. 24th, 2021

Abstract

Gout is one of the common endocrine metabolic disorders. In recent years, the prevalence of gout

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文章引用: 李洁, 杨玉媛, 李海铭, 王忠超. 有关痛风、载脂蛋白 B 以及心血管疾病的研

has increased year by year, and it is easy to be associated with abnormal lipoprotein metabolism, which increases the risk of gout in patients suffering from cardiovascular and cerebrovascular diseases, and is not conducive to the quality of life of gout patients. At the same time, abnormal lipoprotein metabolism is also a risk factor for gout attack and cardiovascular and cerebrovascular diseases, and the three are interrelated. Recent studies have found that patients with gout are associated with abnormal apolipoprotein B, which is better than LDL in predicting cardiovascular disease risk. This paper reviews the relationship between gout, apolipoprotein B and cardiovascular disease.

Keywords

Gout, Apolipoprotein B, Cardiovascular Disease, Atherosclerosis

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1. 引言

21 世纪以来, 随着经济的飞速发展和生活水平的提高, 痛风的患病率逐年增加, 成为常见的代谢疾病[1] [2] [3]。痛风患者易并发脂蛋白代谢异常, 随着痛风患者人数的不断增加, 人们开始关注痛风与脂蛋白等的关系。

脂蛋白代谢异常包括血脂以及载脂蛋白的异常。在脂蛋白成分中, 低密度脂蛋白胆固醇(LDL-C)被认为是致动脉粥样硬化疾病发生发展的主要因素; 然而, 近些年来研究发现, 载脂蛋白 B (Apo B)在预测动脉粥样硬化性心血管疾病发生方面优于 LDL-C [4] [5] [6]。然而, 以往的研究揭示了痛风患者与甘油三酯(TG)、LDL-C 的关系, 但未加阐释痛风患者中 Apo B 的变化及其意义, 故现对痛风、Apo B 以及与心血管疾病的关系进行综述。

2. 痛风与脂蛋白异常

痛风是一种常见的代谢性和炎症性疾病, 因嘌呤代谢失衡, 致使持续升高的血清尿酸超过在其血液或组织中的饱和度, 导致在关节局部形成尿酸钠结晶并沉积, 可引起关节反复疼痛、畸形以及功能障碍 [7] [8] [9]。痛风的患病率在全球各地有很大差异, 发达国家和地区痛风的患病率较高, 发展中国家的患病率相对较低。例如: 2015 年, 痛风在韩国的发病率约 0.76%, 在美国的发病率约为 3.9%, 而在尼日利亚的发病率约为 0.1%。总体而言, 自上世纪九十年代至 2017 年, 痛风的患病率在世界范围内呈现持续增长的状态, 而且男性多于女性, 并随着年龄的增长而加[10] [11] [12] [13]。

痛风患者易合并血脂代谢异常, 其中最常见的高 TG 血症, 但在其它报道中也有 LDL、胆固醇等代谢异常的阐述[14]。而近年来研究发现, 痛风患者中也可见 Apo B 的异常, 例如: Takahashi 等一项回顾性研究发现, 痛风试验组较健康对照组中载 Apo B 的水平增加, 而且差异有统计学意义; 此外, Rasheed 等一项回顾性研究发现, 与单纯的无症状高尿酸血症相比, 痛风患者更容易合并血脂异常, 并且能增加 Apo B 的水平[15] [16]。总之, 痛风的血脂谱中, 除 TG、LDL-C 等是关注的指标外, Apo B 的水平也应该受到重视。

3. Apo B 与心血管疾病

Apo B 在脂蛋白代谢中发挥重要作用, 它是乳糜微粒(CM)、LDL、中密度脂蛋白(IDL)、极低密度脂

蛋白(VLDL)和脂蛋白(a)等致动脉粥样硬化(AS)颗粒的结构蛋白,是对致 AS 颗粒数量的衡量[17] [18]。在致 AS 过程中, Apo B 包裹在这些颗粒的表面,形成完整的结构支架,被动脉内壁捕获,积累于动脉壁内膜,从而启动和促进 AS 发展[19] [20] [21]。

近年来众多研究倾向于 Apo B 比 LDL-C 更能地准确反应致 AS 的风险,在评估 AS 疾病发生、发展方面优于 LDL-C。例如,在 Pencina、Wilkins、Welsh 等的研究中, Apo B 被证明是更准确的致 AS 的风险标志物[22] [23] [24]。传统测量的 LDL,是空腹血液最主要的致 AS 脂蛋白,因此空腹 LDL 水平一直被用于评估 AS 心血管疾病的风险;但是研究发现,尽管使用了降脂类药物,严格控制了 LDL 水平的情况下,仍有一部分的患者发生了心血管疾病;因此,空腹 LDL 水平用来评估心血管疾病的风险具有局限性[17]。

而 Apo B 不受进食的影响,是循环血液中所有致 AS 颗粒或潜在致 AS 颗粒的重要成分,综合了富含 TG 的 VLDL 颗粒和富含胆固醇的 LDL 颗粒引起的 AS 风险。报告显示,当 LDL-C 和 Apo B 不一致时, Apo B 更能指示实际风险[25]。故而, Apo B 被认为是致动脉壁损伤的基本单位,动脉管腔内的 Apo B 颗粒越多,动脉壁内捕获 Apo B 颗粒越多,对动脉壁的损伤就越大;相反,动脉管腔内的 Apo B 颗粒越少,对动脉内壁的损伤就越小,发生心血管疾病的风险就越小。

4. 痛风与心血管疾病

痛风易并发许多疾病,除最常见的血脂异常外,还有心血管疾病等合并症[14]。研究表明,痛风患者罹患心血管疾病的风险增加,高尿酸血症是心血管疾病的独立危险因素,血清尿酸水平升高会增加心力衰竭(HF);与非痛风患者相比,痛风患者罹患冠心病的可能性比其高出 2 倍[26] [27] [28] [29] [30]。因此,针对合并有痛风的心血管疾病的高危患者,降尿酸治疗可获益。例如,在 Thanassoulis 的一项研究中发现, HF 合并痛风的患者是高危人群,血清尿酸水平升高会增加 HF 患者的全因死亡率,使用别嘌醇抑制尿酸后,能改善患者的预后;另外,两项大规模流行病学调查研究表明,痛风患者接受降尿酸治疗后,其心血管死亡风险显著降低[31] [32] [33]。

另外,临床上用于治疗心血管疾病的药物对尿酸代谢也有影响,并且能够促进痛风的发展,例如降压药(赖诺普利)、利尿剂(呋塞米、螺内酯)、降脂药(辛伐他汀)等[14]。因此,针对合并有心血管疾病的痛风患者,应合理应用药物,降低对尿酸代谢的影响,减少痛风发作的频率。

5. 小结

痛风、Apo B 以及心血管疾病三者之间关系密切。痛风能够升高 Apo B 的水平,增加罹患心血管疾病的风险,而 Apo B 的水平可作为循环中衡量致动脉粥样硬化颗粒数量的指标,是评估心血管疾病风险的更好的预测因子。在实际的临床工作中,应该重视 Apo B 的水平,尤其是在痛风及合并有心血管疾病的患者中,降低 Apo B 的水平,改善患者的预后,提高患者的生活质量。

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