

盐替代品对心血管健康影响的研究进展

罗艺, 余强*

重庆医科大学附属第二医院心血管内科/重庆医科大学临床医学系, 重庆

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摘要

心血管疾病(CVD)在21世纪初期已成为全球过早死亡和发病的主要原因, 而预防和控制高血压是阻止心血管疾病发生、发展的核心措施之一。既往大量研究已表明减少食盐摄入可以降低并控制血压, 食用盐替代品——即富含钾或其他类似成分(如 $MgCl_2$, $MgSO_4$ 和 $CaCl_2$ 等)可以作为一种低成本、非药物性降压措施, 但其对心血管疾病的发生、发展及与预后仍有待进一步研究。现就盐替代品对心血管健康影响的研究进行综述, 以期为预防和控制心血管事件提供更具参考价值的信息。

关键词

高血压, 盐替代品, 心血管疾病, 盐摄入

Research Progress on the Impact of Salt Substitutes on Cardiovascular Health

Yi Luo, Qiang She*

Department of Cardiology, The Second Affiliated Hospital of Chongqing Medical University/Department of Clinical Medicine, Chongqing Medical University, Chongqing

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Abstract

Cardiovascular disease (CVD) has become the leading cause of premature death and morbidity in the world at the beginning of the 21st century, the prevention and control of hypertension is one of the core measures to prevent the occurrence and progression of cardiovascular disease. Previous studies have shown that reducing salt intake can lower and control blood pressure. Salt substitutes, which are rich in potassium or other similar ingredients (such as $MgCl_2$, $MgSO_4$, and $CaCl_2$, etc.) can be used as a low-cost, non-pharmacological antihypertensive measure, but their

*通讯作者。

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impact on the occurrence, progression, and prognosis of cardiovascular disease still need further studies. This article reviews the effects of salt substitutes on cardiovascular health to provide more valuable information for the prevention and control of cardiovascular events.

Keywords

Hypertension, Salt Substitutes, Cardiovascular Disease, Salt Intake

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1. 引言

高血压是导致心脑血管疾病的一个主要危险因素。在 1990 年至 2019 年期间, 全球 30 至 79 岁的成年人中高血压患者数量从 6.5 亿增加至 12.8 亿, 且约有 7 亿人并不知道自己是否患有高血压, 其中大多数居住在中等或低收入国家[1] [2]。盐是全球大多数居民饮食中不可或缺的组成部分, 广泛的研究证据表明, 高盐饮食会提高高血压发病率, 并增加心血管事件风险, 例如冠心病、中风、心衰患者液体滞留和症状恶化、左心室肥厚等[3] [4] [5] [6] [7]。低钠盐替代品采用氯化钾部分或全部替代食盐中的钠, 使其钠含量低于标准食盐水平, 从而实现相对较低的钠摄入和更高的钾摄入。本研究旨在探讨富含钾盐替代品的益处、潜在风险以及作为减少膳食钠摄入的公共卫生策略所带来的影响。

2. 对富钾盐替代品的认知和应用

一些针对我国居民人口的研究表明, 与农村地区相比, 城市居民更了解和使用盐替代品。例如, 一项针对中国北方农村的随机分组对照试验[7]发现, 人们对盐替代品的认知度较低, 且相关使用报告较为稀少。另外, Li 等人[8]在中国 5 个省的 120 个乡镇进行了一项大型随机分组试验, 评估社区健康教育和村庄盐替代品对钠摄入量的影响。研究显示, 在干预村庄中, 使用盐替代品的比例明显提高(分别为 62% 和 6%), 相较对照组更多。在受干预的村庄中, 得到价格补贴的盐替代品使用量更高(使用比例分别为 78% 和 48%), 这暗示了价格政策对使用率的影响。

3. 富钾盐替代品对血压的影响

大量的流行病学研究证实了低钠膳食能有效降低血压。例如, 一项涵盖来自 18 个不同国家的 102, 166 名成年人的前瞻性城乡流行病学研究[9]报告了盐摄入量与血压呈正向关联。其结果显示, 每增加 1 克/天的钠摄入量, 血压升高 2.11/0.78 mmHg。特别是在超过 5 g/d 的钠摄入量时, 这种关联变得更为显著, 每增加 1 g/d 的钠摄入量, 血压升高 2.58 mmHg。同时, 像 TOHP-II (高血压预防实验-II)这样的随机对照实验也证实了低盐饮食对血压的非药物干预效果[10] [11]。

另外, 食用盐替代品也能获得相似效果, 通常是通过将食盐中的 NaCl 比例降低 45%~65%, 并用 KCl 或 MgSO₂ 替代, 以达到低钠膳食的目的。一项涵盖 13 个随机对照试验(RCT)的荟萃分析[12]评估了富钾盐替代品代替氯化钠食盐的效果。结果显示, 盐替代品能够显著降低收缩压(平均-5.58 mmHg, 95% CI -7.08 至-4.09 mmHg)和舒张压(平均-2.88 mmHg, 95% CI -3.93 至-1.83 mmHg)。后续的研究也得出了类似的结果, 例如金等人[13]在中国人群上进行的减盐干预荟萃分析, 纳入了 6 项使用盐替代品的随机对照试验, 每项试验持续时间不少于 4 周。结果显示, 盐替代品显著降低了收缩压(平均-5.7 mmHg; 95% CI

-8.5 至 -2.8 mmHg)和舒张压(平均-2.0 mmHg; 95% CI -3.5 至 -0.4 mmHg)。

对于高血压人群,使用富钾盐替代品可能带来更显著的益处。Antonio 等人[14]在秘鲁进行的一项阶梯楔形随机对照实验中发现,基线高血压者的收缩压平均降低了 1.92 mmHg (95% CI 0.54 至 3.29),舒张压平均降低了 1.18 mmHg (95% CI 0.08 至 2.29)。而在无高血压者中,相应的收缩压和舒张压平均降低分别为 1.15 mmHg (95% CI 0.34 至 1.96)和 0.63 mmHg (95% CI -0.01 至 1.28)。至今,针对其他独立因素(例如年龄、性别)的研究暂未发现盐替代品效果存在一致性差异[15] [16]。

4. 心血管事件

在一项针对台北 5 个由退伍军人组成养老院的研究中($n = 1981$),进行了使用富含钾盐(49%氯化钾、49%氯化钠和 2%其他添加剂)的随机对照实验。该实验发现[17],相较于普通盐组,使用富含钾盐替代的群体在心血管疾病死亡率方面降低了 41% (年龄调整 HR 0.59 [95% CI, 0.37~0.95]),但总体死亡率降低并不具有显著性(年龄调整 HR 0.90 [95% CI, 0.79~1.06])。近期的一项荟萃分析报告显示[18],在血压正常的人群中,降低盐摄入量可中等程度地减少全因死亡风险(RR 0.90; 95% CI 0.85~0.95),以及心血管死亡率(RR 0.67; 95% CI 0.46~0.99)。然而,Cocharne 的综述提出了不同的观点[19],目前的临床试验(包括 TOHP 试验[20]、Kwok 等人[21]和 Chang [17]等人的观察随访)不足以证明盐替代品和低盐饮食干预在心血管疾病中的临床重要性。Norm 等[22]对这些临床试验进行的荟萃分析指出心血管事件风险显著下降(RR 0.72; 95% CI 0.59~0.89; 包含 5 个临床试验),同时死亡率风险略有下降(RR 0.89; 95% CI 0.78~1.01; 包含 4 个临床试验),这一证据被认为具有中等强度,支持推荐低钠摄入饮食。此外有研究表明,与平均钠摄入量[23]相比,高钠摄入量与更高的心血管风险和死亡率相关。目前关于低盐摄入与心血管疾病事件之间的关系仍存在争议。一些研究发现钠摄入量与死亡率之间存在 U 型或 J 型关联,这表明过高或过低的钠摄入与死亡风险增加相关[24] [25] [26]。尽管世界高血压联盟指出了这些研究方法上的局限性[27],但目前仍缺乏足够的大规模长期随访临床试验来探索钠摄入与死亡率之间的剂量 - 反应关系,以进一步支持低钠摄入的益处。

心力衰竭作为一种常见慢性疾病,对水、钠摄入量有着更严格的要求。大多数指南建议限制钠摄入量(例如 <3 g/d),以改善患者住院率和死亡率。然而,对于心力衰竭患者是否应控制钠摄入量的证据目前存在不一致性。一项通过分析 HART 的实验数据[28]对 833 名 NYHA II/III 级心力衰竭患者的研究发现,限制钠摄入与死亡和心衰住院风险显著升高相关(42.3% vs 26.2%; HR 1.83; 95% CI, 1.21~2.84; $P = 0.004$),但心血管事件死亡率和全因死亡率无明显升高。而 Colin 等人的研究则得出相反的结论[29]。Vasiliki 等人[30]进行的一项非随机对照试验初步验证了低钠富钾的盐替代品(47% NaCl、40% KCl 和 4% $MgCl_2$)在射血分数降低的(HFrEF)心力衰竭患者中具备一定的安全性,后续需要更多的随机对照试验来进一步研究盐替代品的应用策略。

5. 高钾血症的风险

目前大部分盐替代品主要是指含有 75%氯化钠和 25%氯化钾的配方,与普通盐相比,盐替代品的高膳食钾摄入有助于降低正常血压以及盐敏感人群的血压,并增加一氧化氮(NO)的生物活性[31]。然而,低钠富钾盐替代品所引发的主要担忧在于高钾血症可能带来的不良反应。正常血清钾水平通常介于 3.5 至 5.0 mmol/L 之间,血清钾水平过高会增加不良事件的风险,例如心律失常和心源性猝死。这种风险在合并肾功能不全的患者中尤其值得关注[32]。袁等人进行的研究对 1086 名参与者进行了安全性评估,结果显示盐替代品使用使血清钾水平增加了 0.26 mmol/L,同时导致高钾血症的风险增加了 3.29 倍[33]。另外,一项包括 27 个国际队列[34]的荟萃分析针对慢性肾脏疾病(CKD)预后的研究(共 1,217,986 名参与者)

发现, 高钾血症(>5.5 mmol/L)在普通人群和高心血管风险队列中发生的概率较低(0.49% [95% CI, 0.48~0.50])。

关于膳食钾摄入量和富钾盐替代品与血清钾水平的关系目前尚不清楚。胡等人进行的一项 RCT 关于盐替代品对原发性高血压患者家庭自测血压影响的报告显示, 在 3 个月和 12 个月时, 盐替代品组[35]和普通盐组的血清钾水平没有显著差异。另外, 一些研究并没有进行盐替代品的安全性评估, 这使我们无法得出明确的结论。受试者的临床状态以及钠/钾比率的差异是否会引起高钾血症发生还需要更多的高质量证据来证实。

值得注意的是, 并非所有研究都对盐替代品的安全性进行了评估。是否受试者的临床状态、性别、种族以及钠/钾比率的不同会影响盐替代品在非高血压人群中的安全性和有效性, 这需要更多高质量的证据来加以证实。

6. 小结

过往大量研究表明, 使用富钾盐替代品替代普通食用盐能有效降低血压, 特别是在高血压患者中显示出更为显著的效果。然而, 目前城乡居民对盐替代品的认知存在较大差距。此外, 关于富钾盐对慢性肾病患者血清钾水平、高钾血症发生率以及与心血管疾病事件之间的关系仍存在一些争议。因此, 需要更多大规模临床试验的支持, 以进一步明确盐替代品对心血管疾病患者的益处。

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