科学通报 2025 年 第 70 卷 第 21 期: 3398 ~ 3405
昼夜节律专题 进 展
《中国科学》杂志社 SCIENCE CHINA PRESS

血压的生物钟调节

陈梦月, 陈苗, 傅舒凝, 陈压西, 阮雄中*

重庆医科大学感染病性疾病与分子生物教育部重点实验室, 重庆市脂糖代谢重点实验室, 重庆 400016
* 联系人, E-mail: x.ruan@ucl.ac.uk

2024-07-10 收稿, 2024-10-06 修回, 2024-10-11 接受, 2024-10-17 网络版发表
国家自然科学基金(32400943)资助

摘要 心脑血管疾病(cardio-cerebrovascular disease, CVD)是导致全球人类死亡的首要原因. 高血压是CVD最主要可改变的风险因素, 血压异常包含血压数值异常及血压昼夜节律异常, 且血压昼夜节律异常的CVD患者死亡率高于血压昼夜节律正常者. 尽管目前的研究已经发现众多血压调节机制, 但无论是在动物模型还是人群研究中, 生物钟在血压中的作用都缺乏更多的研究和重视. 本文总结了生物钟系统、行为与环境以及其他各项因素(疾病、种族等)对血压昼夜节律的综合影响, 重点阐述此领域昼夜节律与血压调节的最新串扰机制, 并对血压相关疾病的时间疗法进行展望.

关键词 昼夜节律, 血压, 高血压, 心脑血管疾病, 时钟基因

心脑血管疾病(cardio-cerebrovascular disease, CVD)是所有与血管病变有关的心脑疾病的总称, 其年死亡人数可占全球死亡总数的30%以上, 是全球人类首位的死亡原因[1]. 在我国, CVD年死亡率呈逐年上升趋势[2]. 高血压是CVD最主要可改变的高风险因素, 因此, 需清楚了解其内源性和外源性影响因素, 以减少CVD发病率[3]. 血压异常是直接影响高血压的关键因素, 血压每日波动是人类最佳及研究最多的生理节律之一. 除了血压数值异常外, 血压昼夜节律紊乱也是关键但却非常容易被忽略的指标. 相比于血压数值异常升高, 夜间血压升高导致的昼夜节律异常被认为是CVD更有效且独立的预测指标, 且血压节律异常的CVD患者死亡率更高[4].

24 h动态血压监测是目前临床上诊断血压昼夜节律紊乱的金标准. 在接受治疗的高血压患者中, 血压昼夜节律紊乱的发生率可达80%以上[5]. 但因动态监测技术的普及有限, 导致大量患者不能被及时诊断, 极易暴露在较高心血管风险中, 同时造成血压昼夜节律的重要性和危害性被大众忽略, 以此进入恶性循环. 本文结合最新研究进展, 从生物钟机制、血压昼夜波动类型、生物钟与血压节律调控等进行切入总结, 并对高血压的时间疗法进行展望.

1 生物节律机制

生物节律影响生命体的生理和行为等多个方面. 18世纪法国物理学家Jean-Jacques发现, 即使在没有外部时间线索的情况下, 生物体也产生了大约24 h的生物节律. 1938年, Nathaniel揭示人类受到内在昼夜节律的强烈影响. 20世纪70年代初, 人们发现下丘脑中的视交叉上核(suprachiasmatic nucleus, SCN)是协调昼夜节律的中央昼夜节律起搏器[6]. 随后, 遗传学研究发现, 由时钟基因组成的分子转录-翻译反馈环, 使细胞能够自主地发挥24 h时钟功能. 在哺乳动物中, Bmal1(brain and muscle ARNT-like protein 1)和Clock(circadian locomotor output cycles kap)形成异物二聚体, 可结合到靶基因激活子的特异性DNA区域E-box上并启动下

引用格式: 陈梦月, 陈苗, 傅舒凝, 等. 血压的生物钟调节. 科学通报, 2025, 70: 3398–3405
Chen M Y, Miao M, Fu S N, et al. Biological clock regulation of blood pressure (in Chinese). Chin Sci Bull, 2025, 70: 3398–3405, doi: 10.1360/TB-2024-0733

游的基因转录, 如Pers(periods)、Crys(cryptochromes)及时钟控制基因. Pers和Crys积累达到临界浓度时, 抑制Bmal1/Clock的转录激活. 当Pers和Crys浓度下降, 此24 h循环便可重新开始. 除了该核心反馈环, 2个核受体亚家族, Rev-erb和RORs家族共同作为昼夜节律的关键组件发挥作用. Clock/Bmal1二聚体可增强Clock启动子活性, 而DEC1(differentiated embryo-chondrocyte gene 1, DEC1)可通过与Clock元件E-box竞争性结合, 从而抑制Clock/Bmal1增强的启动子活性. 此外, 时钟基因还可调节各器官组织中的时钟控制基因, 进而影响机体各项功能. 2017年诺贝尔生理学或医学奖对此工作进行了表彰[7]. 20世纪90年代, 有关昼夜节律的研究发生进一步突破, 研究人员发现昼夜节律系统不仅受中央起搏器调控, 而且是在几乎每个器官、组织甚至细胞都存在同样的分子机制[8]. 自此, 昼夜节律系统更全面地被熟知为由SCN的中央起搏器以及全身器官、组织和细胞中的外周振荡器共同组成, 日后持续更多的相关研究定会使节律系统的调节机制更为完善和清晰.

2 血压的昼夜节律

根据昼夜波动程度, 血压可以分为杓型血压、非杓型血压、反杓型血压和超杓型血压等类型. 杓型血压变化的特征是, 与白天血压相比, 夜间血压下降幅度达到10%~20%, 形成一个明显的“勺形”曲线; 非杓型血压变化则显示夜间血压下降幅度较小, 通常小于10%; 反杓型血压变化指的是夜间血压没有任何下降, 甚至可能上升; 超杓型血压是夜间血压下降幅度过大, 与白天相比下降大于20%[9].

非杓型和反杓型血压属于夜间高血压类型, 此类型危害极大, 可独立于日间血压预测CVD死亡. 夜间高血压定义为夜间平均收缩压≥120 mmHg和/或平均舒张压≥70 mmHg, 包括: 单纯性夜间高血压; 白天-黑夜持续性高血压; 其他: (1) 直立性低血压合并仰卧位夜间高血压; (2) 因药物疗效不能维持24 h而发生无法控制的夜间高血压; (3) 夜间高血压延续到清晨发展为晨间高血压. 杓型血压为正常生理状态血压, 非杓型、超杓型及反杓型血压均为血压昼夜节律紊乱[10]. 此外, 清晨血压激增也会导致血压昼夜节律改变, 可分为晨峰血压型和夜间持续晨间高血压, 此血压类型仍会明显增加CVD风险[11](图1). 2019年, 亚洲动态血压监测HOPE专家共识提出“血压最佳24 h控制”: 降低24 h血压、维持正常血压昼夜节律和减小异常血压变异(尤其是晨峰血压), 这是治疗心血管事件的最佳思路[12]. 2023年, 中国高血压联盟组织王继光等专家共同撰写《夜间高血压管理中国专家共识》[4], 是目前少有的专门针对夜间高血压的共识; 2024年, 中国高血压联盟再次组织专家撰写了《高血压患者高质量血压管理中国专家建议》[13], 再次强调维持血压正常节律、高质量管理夜间及晨峰高血压患者的重要性. 以上共识的发表, 不仅代表人们对血压昼夜节律的逐渐重视, 也为科研人员进一步研究血压昼夜节律提供了理论基础.

3 血压昼夜节律的调控因素

血压的昼夜节律是内源性昼夜节律机制、24 h环境和行为及体内健康状况、种族和遗传差异等共同调控结果[14]. 除生物钟调节系统所包含的主时钟和外周时钟外, 光照/黑暗、睡眠/清醒、进食/禁食、活动/休息、精神压力、体温、体位和年龄等环境和行为因素, 以及其他因素如遗传、饮食习惯(高盐)、继发性疾病等, 通过对神经传递、肾素-血管紧张素-醛固酮系统(renin angiotensin aldosterone system, RAAS)、血管内皮反应、交感神经和迷走神经调节、肾脏功能、心脏功能、肌源性反应、免疫等器官或系统调节, 最终共同影响血压昼夜节律波动. 这些器官或系统几乎都存在昼夜节律表达并受到生物钟调控. 如交感和副交感神经系统在血压昼夜节律的波动中扮演着重要角色; 许多激素例如肾上腺素、去甲肾上腺素、褪黑素等, 它们自身都受到生物钟的控制, 并调节着血压; 血管收缩因子内皮素1(endothelin-1, ET-1)具有明显的昼夜节律表达, 也参与血压昼夜节律的调节; 肾脏中肾小球滤过率、尿渗透压、尿电解质排泄都具有昼夜节律表达, 这些功能均与血压昼夜节律密切相关[15,16](图2). 由于调节血压的固有系统已被大众熟知, 故本文后续不对此进行重点阐述, 而将重点总结和展望时钟基因、行为与环境等与血压昼夜节律机制之间的串扰.

3.1 时钟基因与血压昼夜节律的串扰

大量动物模型研究表明, 时钟基因在血压调节方面发挥着重要作用. 其中, Bmal1与Per1在血压及血压节律中的作用尤为突出, 时钟基因不仅可以作为生物钟的关键组分影响血压数值, 也能发挥节律功能影响血压昼夜节律.

Curtis等人[17]表明, Bmal1雄性敲除小鼠的血压降

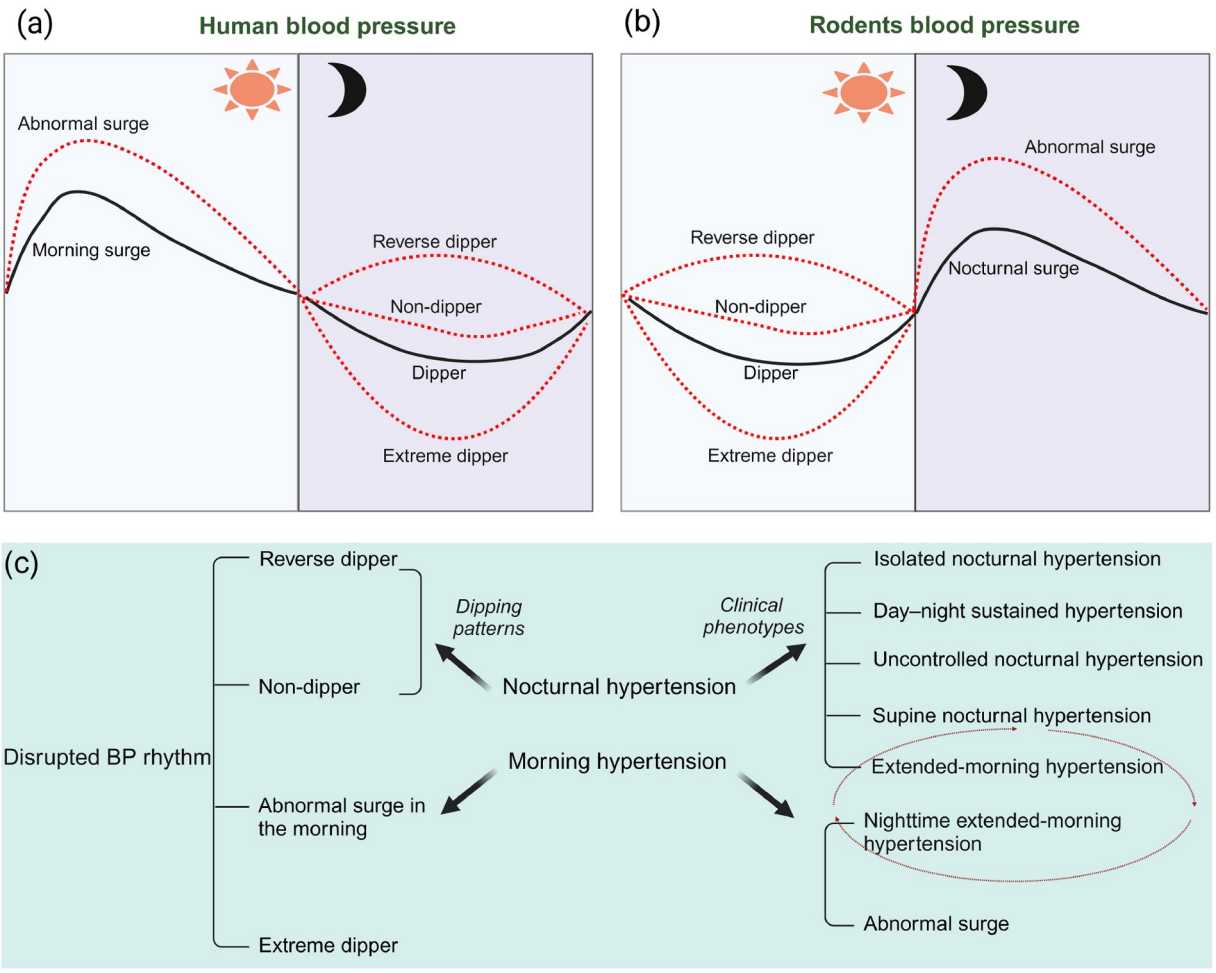

图 1 人类和啮齿动物血压昼夜节律波动示意图. (a) 人类血压昼夜节律; (b) 啮齿动物血压昼夜节律; (c) 血压昼夜波动类型、夜间高血压、晨间高血压及其临床分类关系示意图. 图片素材来源于BioRender.com

Figure 1 Schematic diagram of blood pressure circadian fluctuations in humans and rodents. (a) Circadian rhythm of blood pressure in human; (b) circadian rhythm of blood pressure in rodents; (c) diurnal blood pressure fluctuation type, nocturnal hypertension, morning hypertension and their clinical classification relationship diagram. Figure was created with BioRender.com

低且出现血压节律减弱. 随后, Anea等人[18]发现, Bmal1雄性敲除小鼠的血压节律紊乱与内皮NO合酶的解偶联和超氧化物水平升高有关. 2018年Chang等人[19]报道, 当血管周围脂肪中Bmal1缺失时会导致小鼠静息期血压下降, 这一发现为临床治疗高血压提供了靶向时钟基因指标. 新近, Huo等人[20]的研究表明, Bmal1作为生物钟的关键成分在维持血管稳态方面发挥着重要作用, 其缺失可能通过增强血管重塑并促进血压升高; 雄性Bmal1肾脏特异性敲除小鼠的血压较低, 并且Bmal1在低钾高盐饮食引起的血压升高和促炎环境中起血压调节保护作用[21]. 不仅如此, Costello等人[22]在2023年新发现, 肾上腺Bmal1在调节血压节律、小鼠活动节律、钠钾时间平衡与血清皮质酮昼夜节律中同样发挥关键作用. 这些研究证实, Bmal1对血压数值及血压昼夜节律的影响都意义重大.

Per1在血压稳态中同样扮演不可或缺的角色. 早期, Solocinski等人[23]证实Per1在肾脏钠稳态中发挥重要作用, 从而影响血压稳态; 在此基础上, 进一步证实, 小鼠中Per1缺失导致静息期血压明显高于对照组[24]; 另一研究也表明Per1正向调节肾脏上皮细胞钠离子通道蛋白-α(epithelial sodium channel-α, αENaC)启动子的转录激活并调节血压昼夜节律[25]; Zietara等人[26]的研究证明, 高血压模型大鼠中Per1缺失会导致血压昼夜节律改变、血浆醛固酮水平升高以及高血压恶化和肾

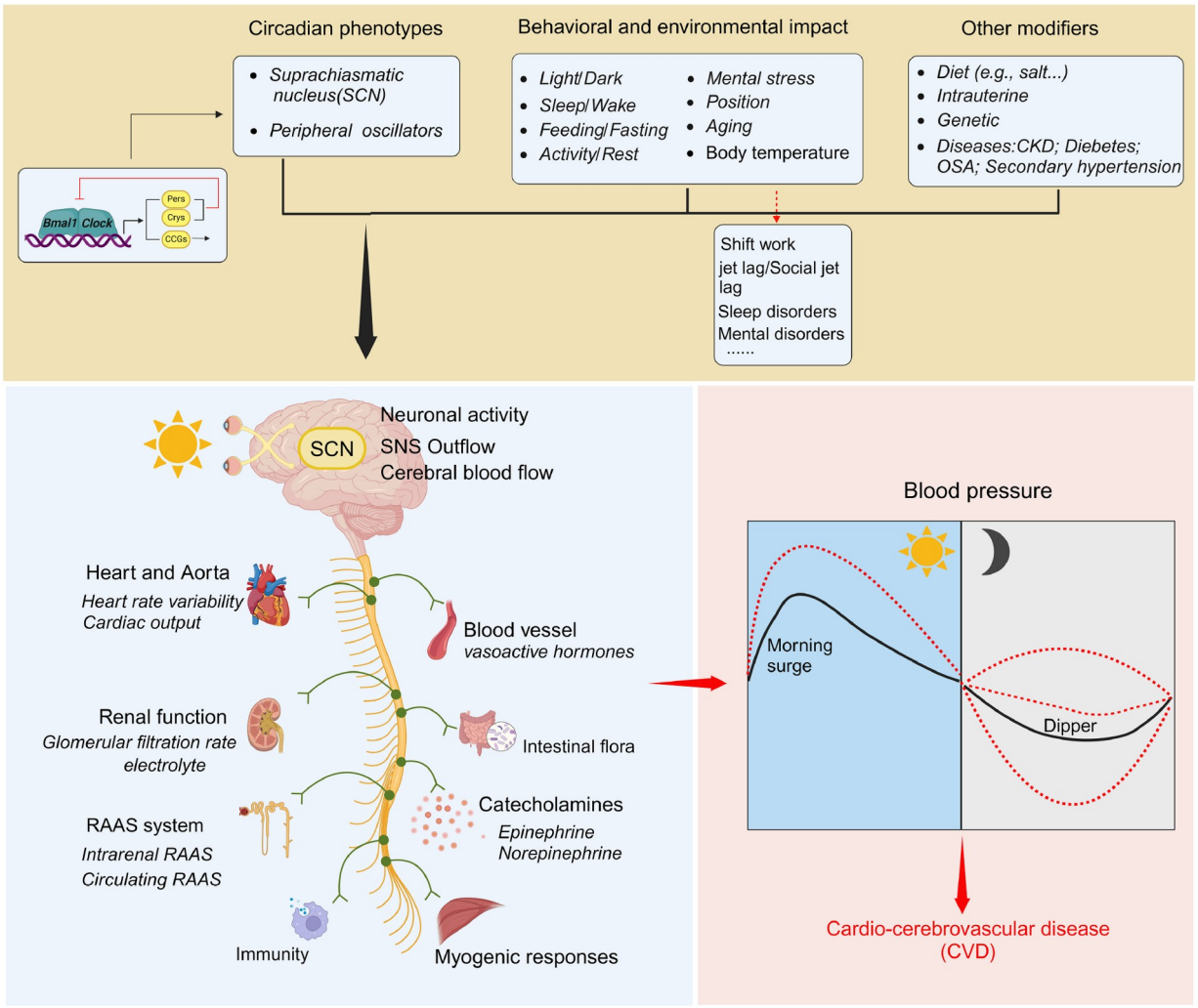

图 2 血压的生物钟调节机制示意图. 昼夜节律、环境和行为及其他因素等相互作用, 通过影响血压的调节器官或系统, 最终导致血压节律紊乱, 增加CVD风险. 细节见文中所述. 图片素材来源于BioRender.com

Figure 2 Schematic diagram of biological clock regulation mechanism of blood pressure. The interaction of circadian rhythm, environmental and behavioral factors, and other factors, by affecting the organ or system that regulates blood pressure, ultimately leads to the disturbance of blood pressure rhythm and increases the risk of CVD. Please see the text for details. Figure was created with BioRender.com

损伤增加, 这突出了Per1是连接生物钟与RAAS系统的重要成分; Mingli He等人[27]借助自发性高血压大鼠模型, 发现Per1基因中的rs225380突变与血压下降之间存在联系.

其他时钟基因与血压之间也存在密切联系. Soliman等人[28]报道Clock缺失小鼠的血压显著降低并出现轻度尿崩症, 并证实生物钟可通过影响肾脏钠节律从而影响血压; 另有发现, DEC1和Clock: Bmal1可共同调节编码Na^+/K^+-ATP酶β1亚单位的基因—ATP1B1的昼夜节律表达从而调节血压昼夜节律[29]; 研究报道肾上腺Cry1和Cry2双敲除小鼠出现了盐敏感性高血压, 此研究再次强调肾上腺生物钟可对血压发挥重要的调节作用[30]; Cry1遗传变异可能与血压升高和高血压的发生密切相关[31]. 这些研究提示, 生物钟调节血压节律的机制是复杂的: 时钟基因既可以单纯地影响血压数值, 同时也能影响其昼夜节律, 且时钟基因可互相影响, 在研究时可注意更系统和全面地观察生物钟反馈环的改变.

3.2 饮食、行为及环境等对血压昼夜节律的调节

3.2.1 进食时间与血压节律

在最近的研究中发现, 进食时间可以调节血压昼

夜节律. Zhang等人[32]发现, 在小鼠非活动期喂食, 会导致其血压昼夜节律发生逆转性改变. 这项发现对轮班工人、国际旅行等夜间进食人群的血压昼夜节律紊乱有突破性意义. Hou等人[33]表明, 若仅在活跃期给与糖尿病小鼠食物, 可恢复糖尿病小鼠的血压昼夜节律. 这一发现揭示了食物摄入时间在糖尿病血压昼夜节律中的潜在治疗作用, 通过限制糖尿病患者在正确的时间进食或可改善其血压节律损害情况. 针对这一发现, 后续研究或许可以探讨进食时间是否能缓解其他疾病状态下的血压昼夜节律紊乱.

3.2.2 *时差/社会时差、轮班工作与血压节律*

社会时差是由于人们工作日的睡眠习惯与周末或节假日的睡眠习惯存在显著差异, 导致人们在生物钟和社会活动之间产生的时差现象, 这已成为一种极其普遍的现象[34]. Pompeia等人[35]证实, 存在较大社交时差的青少年, 在心血管代谢方面表现出更多的不良潜在特征, 如血压、血糖、血脂水平等方面异常, 从而增加CVD风险.

轮班工作可能导致血压昼夜节律紊乱. Riegel等人[36]发现, 轮班工作的员工在睡眠不足时, 使用高血压药物的比例更高. Toffoli等人[37]发现, 夜班工作显著增加夜间血压, 同时发生血压昼夜节律失调. Lunde等人[38]发现, 轮班工作与心血管疾病发生相关, 这可能是由于昼夜节律被打乱导致激素变化和代谢紊乱, 从而导致CVD发生. Kanki等人[39]通过生物库350,000名人类参与者样本, 证明了短睡眠(<5 h)和长睡眠(>8 h)、睡眠质量受损或长期夜班工作与血压之间存在正相关, 保持适当的睡眠时间可能是降低患高血压风险的非常规方法. 缓解轮班工作导致的节律紊乱对广大夜班人群的身体健康十分重要, Kanki的发现为降低轮班工作人群的心血管事件风险提供了非药物主导的新思路, 日后的研究可以从更多非药物方式(如饮食等)探索如何改善轮班工作人群血压节律紊乱.

3.2.3 *肠道与免疫*

越来越多的途径被报道与血压昼夜节律调控相关, 如肠道菌群及免疫系统. Chakraborty等人[40]在大鼠中观察到, 微生物群芳香族氨基酸生物合成与降解与血压节律有关, 该发现为微生物靶向高血压提供了基础. Güntürk等人[41]发现高血压患者的血浆IL-18水平增加, 且与血压夜间不下降有关. 系统性红斑狼疮患者的血压和免疫激活标志物会明显增加, 并且这类人群易出现夜间高血压现象[42]. 尽管目前有关血压昼夜节律机制与肠道、免疫系统的研究不如其他系统完善, 但仍提示血压昼夜节律的调节十分复杂, 还有大量空白等待探索.

3.3 其他因素

研究表明, 合并其他疾病会显著增加血压节律紊乱风险, 如高血压合并慢性肾脏疾病、肥胖、糖尿病、睡眠呼吸暂停综合征等[43]; 我国高钠饮食人群较多, 这可能是导致夜间高血压控制率显著低于欧美人群的原因, 同时也与晨峰高血压相关[44,45]; 另外, 遗传、用药疗效等均会影响血压昼夜节律[46]. 由此可见, 血压昼夜节律的影响因素众多, 或需从更多不同的角度去发掘其调控机制.

4 高血压时间疗法

尽管降血压药物取得了进展, 但CVD死亡率仍稳居疾病首位. 因此, 目前仍亟须进一步加深对高血压机制的理解以提升高血压治疗效果. 时间疗法指根据生物节律在不同时段给药, 以期获取最大疗效的治疗策略. 血压相关疾病的时间疗法则可通过非药物干预(例如进餐时间)和药物时间治疗来预防和控制CVD发生[47]. 目前已经有许多临床研究来评估不同时间服用降压药物的有效性, 但结果并不一致. Mathur等人[48]发现晚上睡前服用抗高血压药物能更有效地控制夜间和清晨高血压. 而Kreutz等人[49]表明血压药物不应在睡前给药, 睡前给药可能带来的不利影响, 如夜间血压过低. 这项研究建议, 在选择给药时间时需要考虑患者的具体情况, 以及所用药物的药代动力学及半衰期等, 以达到更好控制血压并减少心血管事件风险的目的. 因临床研究耗时长、体量大, 目前, 高血压的时间疗法研究仍较缺乏. 不同的疾病类型、病人年龄、药物品种等都增加了时间疗法的应用难度, 还需大量的临床研究和证据来完善此方法, 对于科研人员来说, 既是挑战也是任务.

5 总结

血压昼夜节律的改变与严重心脑血管风险增加相关, 了解血压正常人群、高血压前人群和高血压患者血压昼夜波动与生物钟机制、行为和环境因素等之间的关系, 并据此寻找出更有效的治疗手段有助于减少人类CVD的死亡率. 未来的研究希望能将血压昼夜节律调节机制丰富并完善, 将时间疗法扎根于基础, 应用于临床, 为预防及治疗高血压提供更有效的策略.

参考文献

1 Wang C, Hou X, Guan Q, et al. RNA modification in cardiovascular disease: Implications for therapeutic interventions. Sig Transduct Target Ther, 2023, 8: 412

2 Miao L P, Ren K H, Li M D, et al. Trend analysis and prediction of cardiovascular disease mortality in China from 2009 to 2021 (in Chinese). Chin Gen Pract, 2024, 27: 2260–2264 [苗立鹏, 任柯好, 李梦蝶, 等. 2009~2021年中国心血管疾病死亡趋势分析与预测研究. 中国全科医学, 2024, 27: 2260–2264]

3 Fan F, David Spence J, Huo Y. Beyond hypertension: Hypertension with hyperhomocysteinemia. Sci Bull, 2023, 68: 1975–1977

4 Liu J, Li Y, Zhang X, et al. Management of nocturnal hypertension: An expert consensus document from Chinese Hypertension League. J Clin Hypertens, 2024, 26: 71–83

5 Banegas J R, Ruilope L M, de la Sierra A, et al. High prevalence of masked uncontrolled hypertension in people with treated hypertension. Eur Heart J, 2014, 35: 3304–3312

6 Lu Q, Kim J Y. Mammalian circadian networks mediated by the suprachiasmatic nucleus. FEBS J, 2022, 289: 6589–6604

7 Nelson R J, Bumgarner J R, Liu J A, et al. Time of day as a critical variable in biology. BMC Biol, 2022, 20: 142

8 Wang Y, Guo H, He F. Circadian disruption: From mouse models to molecular mechanisms and cancer therapeutic targets. Cancer Metastasis Rev, 2023, 42: 297–322

9 Mancia G, Facchetti R, Bombelli M, et al. Short- and long-term reproducibility of nighttime blood pressure phenotypes and nocturnal blood pressure reduction. Hypertension, 2021, 77: 1745–1755

10 Mancia G, Kreutz R, Brunström M, et al. 2023 ESH guidelines for the management of arterial hypertension the task force for the management of arterial hypertension of the European Society of Hypertension. J Hypertens, 2023, 41: 1874–2071

11 Filippone E J, Foy A J, Naccarelli G V. Controversies in hypertension III: Dipping, nocturnal hypertension, and the morning surge. Am J Med, 2023, 136: 629–637

12 Kario K, Hoshide S, Chia Y C, et al. Guidance on ambulatory blood pressure monitoring: A statement from the HOPE Asia Network. J Clin Hypertens, 2021, 23: 411–421

13 Chinese Expert Recommendations on High-quality Blood Pressure Management for Hypertensive Patients by Chinese Hypertension Alliance, Chen X, Wang J G, et al. Chinese expert recommendations for high-quality blood pressure management in patients with hypertension (in Chinese). Chin J Hypertens, 2024, 32: 104–111 [中国高血压联盟《高血压患者高质量血压管理中国专家建议》委员会, 陈歆, 王继光, 等. 高血压患者高质量血压管理中国专家建议. 中华高血压杂志. 2024, 32: 104–111]

14 Chellappa S L, Vujovic N, Williams J S, et al. Impact of circadian disruption on cardiovascular function and disease. Trends Endocrinol Metab, 2019, 30: 767–779

15 Shafer B M, Kogan S A, McHill A W. Pressure building against the clock: The impact of circadian misalignment on blood pressure. Curr Hypertens Rep, 2024, 26: 31–42

16 Smolensky M H, Hermida R C, Portaluppi F. Circadian mechanisms of 24-hour blood pressure regulation and patterning. Sleep Med Rev, 2017, 33: 4–16

17 Curtis A M, Cheng Y, Kapoor S, et al. Circadian variation of blood pressure and the vascular response to asynchronous stress. Proc Natl Acad Sci USA, 2007, 104: 3450–3455

18 Anea C B, Cheng B, Sharma S, et al. Increased superoxide and endothelial NO synthase uncoupling in blood vessels of Bmal1-knockout mice. Circ Res, 2012, 111: 1157–1165

19 Chang L, Xiong W, Zhao X, et al. Bmal1 in perivascular adipose tissue regulates resting-phase blood pressure through transcriptional regulation of angiotensinogen. Circulation, 2018, 138: 67–79

20 Huo M, Cao X, Zhang H, et al. Loss of myeloid Bmal1 exacerbates hypertensive vascular remodelling through interaction with STAT6 in mice. Cardiovasc Res, 2022, 118: 2859–2874

21 Crislip G R, Costello H M, Juffre A, et al. Male kidney-specific BMAL1 knockout mice are protected from K^+-deficient, high-salt diet-induced blood pressure increases. Am J Physiol Renal Physiol, 2023, 325: F656–F668

22 Costello H M, Crislip G R, Cheng K Y, et al. Adrenal-specific KO of the circadian clock protein BMAL1 alters blood pressure rhythm and timing of eating behavior. Function, 2023, 4: zqad001

23 Solocinski K, Richards J, All S, et al. Transcriptional regulation of NHE3 and SGLT1 by the circadian clock protein Per1 in proximal tubule cells. Am J Physiol Renal Physiol, 2015, 309: F933–F942

24 Solocinski K, Holzworth M, Wen X, et al. Desoxycorticosterone pivalate-salt treatment leads to non-dipping hypertension in Per1 knockout mice. Acta Physiol, 2017, 220: 72–82

25 Alli A, Yu L, Holzworth M, et al. Direct and indirect inhibition of the circadian clock protein Per1: Effects on ENaC and blood pressure. Am J Physiol Renal Physiol, 2019, 316: F807–F813

26 Zietara A, Spires D R, Juffre A, et al. Knockout of the circadian clock protein PER1 (Period1) exacerbates hypertension and increases kidney injury in Dahl salt-sensitive rats. Hypertension, 2022, 79: 2519–2529

27 He M, Li L, Li J, et al. rs2253820 variant controls blood pressure dip after stroke by increasing CLOCK–BMAL1 expression. Transl Stroke Res, 2023, 14: 472–489

28 Soliman R H, Pollock D M. Circadian control of sodium and blood pressure regulation. Am J Hypertens, 2021, 34: 1130–1142

29 Nakashima A, Kawamoto T, Noshiro M, et al. Dec1 and CLOCK regulate Na^+/K^+-ATPase β1 subunit expression and blood pressure. Hypertension, 2018, 72: 746–754

30 Doi M, Takahashi Y, Komatsu R, et al. Salt-sensitive hypertension in circadian clock–deficient cry-null mice involves dysregulated adrenal Hsd3b6. Nat Med, 2010, 16: 67–74

31 Firouzabadi F D, Mirzababaei A, Shiraseb F, et al. The interaction between CRY1 Polymorphism and Alternative Healthy Eating Index (AHEI) on cardiovascular risk factors in overweight women and women with obesity: A cross-sectional study. BMC Endocr Disord, 2023, 23: 172

32 Zhang D, Colson J C, Jin C, et al. Timing of food intake drives the circadian rhythm of blood pressure. Function, 2021, 2: zqaa034

33 Hou T, Su W, Duncan M J, et al. Time-restricted feeding protects the blood pressure circadian rhythm in diabetic mice. Proc Natl Acad Sci USA, 2021, 118: e2015873118

34 Caliandro R, Streng A A, van Kerkhof L W M, et al. Social jetlag and related risks for human health: A timely review. Nutrients, 2021, 13: 4543

35 Pompeia S, Panjeh S, Louzada F M, et al. Social jetlag is associated with adverse cardiometabolic latent traits in early adolescence: An observational study. Front Endocrinol, 2023, 14: 1085302

36 Riegel B, Daus M, Lozano A J, et al. Shift workers have higher blood pressure medicine use, but only when they are short sleepers: A longitudinal UK biobank study. J Am Heart Assoc, 2019, 8: e013269

37 Toffoli B, Tonon F, Giudici F, et al. Preliminary study on the effect of a night shift on blood pressure and clock gene expression. Int J Mol Sci, 2023, 24: 9309

38 Lunde L K, Skare Ø, Mamen A, et al. Cardiovascular health effects of shift work with long working hours and night shifts: Study protocol for a three-year prospective follow-up study on industrial workers. Int J Environ Res Public Health, 2020, 17: 589

39 Kanki M, Nath A P, Xiang R, et al. Poor sleep and shift work associate with increased blood pressure and inflammation in UK Biobank participants. Nat Commun, 2023, 14: 7096

40 Chakraborty S, Mandal J, Cheng X, et al. Diurnal timing dependent alterations in gut microbial composition are synchronously linked to salt-sensitive hypertension and renal damage. Hypertension, 2020, 76: 59–72

41 Güntürk E E, Güntürk İ, Topuz A N, et al. Serum interleukin-18 levels are associated with non-dipping pattern in newly diagnosed hypertensive patients. Blood Pressure Monitoring, 2021, 26: 87–92

42 Carranza-Leon D A, Oeser A, Wu Q, et al. Ambulatory blood pressure in patients with systemic lupus erythematosus: Association with markers of immune activation. Lupus, 2020, 29: 1683–1690

43 Fu X, Ren H, Xie J, et al. Association of nighttime masked uncontrolled hypertension with left ventricular hypertrophy and kidney function among patients with chronic kidney disease not receiving dialysis. JAMA Netw Open, 2022, 5: e2214460

44 Gupta D K, Lewis C E, Varady K A, et al. Effect of dietary sodium on blood pressure. JAMA, 2023, 330: 2258–2266

45 Xue X -, Li W, Xie M -, et al. High sodium diet intake and cardiovascular diseases: An attributable death study in Tianjin, China. J Clin Hypertens, 2023, 25: 30–37

46 Eckle T, Bertazzo J, Khatua T N, et al. Circadian influences on myocardial ischemia-reperfusion injury and heart failure. Circ Res, 2024, 134: 675–694

47 Gumz M L, Shimbo D, Abdalla M, et al. Toward precision medicine: circadian rhythm of blood pressure and chronotherapy for hypertension – 2021 NHLBI workshop report. Hypertension, 2023, 80: 503–522

48 Mathur P, Kadavath S, Marsh J D, et al. Chronotherapy for hypertension: Improvement in patient outcomes with bedtime administration of antihypertensive drugs. Eur Heart J, 2020, 41: 4577–4579

49 Kreutz R, Kjeldsen S E, Burnier M, et al. Blood pressure medication should not be routinely dosed at bedtime. We must disregard the data from the HYGIA project. Blood Pressure, 2020, 29: 135–136

Summary for “血压的生物钟调节”

Biological clock regulation of blood pressure

Mengyue Chen, Chen Miao, Shuning Fu, Yaxi Chen & Xiongzhong Ruan*

Centre for Lipid Research & Chongqing Key Laboratory of Metabolism on Lipid and Glucose, Key Laboratory of Molecular Biology for Infectious Diseases (Ministry of Education), Institute for Viral Hepatitis, Department of Infectious Diseases, the Second Affiliated Hospital, Chongqing Medical University, Chongqing 400016, China

* Corresponding author, E-mail: x.ruan@ucl.ac.uk

Cardiovascular and cerebrovascular diseases (CVDs) are the leading cause of death worldwide. The global annual death rate from CVD is increasing annually. Hypertension is the most readily modifiable risk factor for CVD; therefore, a clear understanding of the endogenous and exogenous factors influencing hypertension is needed to reduce the incidence of CVD. Abnormal blood pressure is the key factor that directly affects hypertension, and its diurnal fluctuation is one of the most commonly and thoroughly studied physiological rhythms in humans. Abnormal circadian rhythms due to elevated blood pressure at night are considered to be more effective and independent predictors of CVD than abnormal blood pressure values are, and the mortality rate is relatively higher in CVD patients with abnormal blood pressure rhythms. At present, nocturnal hypertension is highly prevalent in the Chinese population and other Asian populations, but many research gaps exist in with regard to the pathogenesis and treatment. Twenty-four-hour ambulatory blood pressure (BP) monitoring is currently the gold standard for the clinical diagnosis of blood pressure circadian rhythm disorders, but routine office or home BP measurement is still the measurement method preferred by the public. The popularity of dynamic monitoring technology is limited, resulting in a large number of patients who are not diagnosed in a timely manner and are consequently at high risk for CVD. The importance of and potential risks associated with abnormal blood pressure circadian rhythms are ignored by the public. On the basis of the latest progress in research, this paper summarizes the process by which biorhythms develop and their specific regulatory mechanism for the first time and then introduces various types of diurnal blood pressure fluctuations and their correlation with diseases. In particular, the harmful effects of nocturnal hypertension caused by an abnormal increase in nocturnal blood pressure, specifically the contributions to cardiovascular and cerebrovascular diseases, are emphasized, and the current gaps in and status of research are discussed. The comprehensive factors influencing blood pressure rhythms are then summarized, and the cross-talk mechanism between the biological clock and blood pressure rhythms are summarized with regard to clock genes, the timing of meals, the performance of shift work, immune factors, intestinal flora, genetics, and diet (high salt). Finally, the status of research on and clinical application of chronotherapy for hypertension generated by circadian rhythms are discussed. The aim of this study is to explore the harm caused by diseases resulting from disturbances in blood pressure rhythms, enrich the understanding of CVD pathogenesis, and provide a theoretical basis for reducing the increased risk of CVD.

circadian rhythm, blood pressure, hypertension, cardiovascular and cerebrovascular diseases, clock genes

doi: 10.1360/TB-2024-0733