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高原心脏病发病机制及治疗研究进展

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【摘要】 高海拔地区氧分压较低,长期暴露在高海拔地区,机体会处于低压低氧状态。低压低氧会激发机体内多种机制,影响机体正常运行。机体对低氧的主要反应之一是低氧性肺血管收缩(hypoxic pulmonary vasoconstriction,HPV)。当 HPV 加重时会诱发高原心脏病(high altitude heart disease,HAHD)。HAHD 是慢性高原病(chronic high altitude disease,CHAD)的一种临床分型,其主要特征是血管收缩和肺动脉过度增殖性重塑,肺动脉压力持续升高,进一步增加右心后负荷,引起右心室肥厚,最终导致右心衰。虽然近些年相关领域人员对 HAHD 研究不断深入,但其患病率仍然很高。科研人员一直致力于寻找 HAHD 的理想治疗方法,但这是一个巨大的挑战。尤其是 HAHD 亚型,对其知者甚少。现就近几年对 HAHD 发病机制及治疗方面的研究进行综述,以期为预防和治疗 HAHD 提供新的线索。

【关键词】 高原心脏病;肺动脉高压;低压低氧;血管重塑;发病机制;治疗
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Research progress on the pathogenesis and treatment of high altitude heart disease

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【Abstract】 The oxygen partial pressure in high-altitude areas is low. Long-term exposure to high-altitude areas leads to a state of low-pressure hypoxia. The combination of low pressure and oxygen levels triggers a variety of mechanisms that disrupt normal bodily functions. One key response to hypoxia is hypoxic pulmonary vasoconstriction, which, when aggravated, can induce the development of high altitude heart disease (HAHD). HAHD is a clinical type of chronic mountain sickness mainly characterized by vasoconstriction and hyperproliferative remodeling of the

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pulmonary artery. As the pressure in the pulmonary artery continues to rise, it increases the posterior load on the right heart, causing right ventricular hypertrophy. Over time, this can lead to right heart failure or even complete heart failure. Despite extensive on HAHD in recent years, its prevalence remains high. While researchers are committed to finding an ideal treatment, this remains a huge challenge, particularly as awareness of the HAHD subtype is still limited. Here, we review the recent research on the pathogenesis and treatment of HAHD, with the aim of providing new clues for its prevention and treatment.

【**Keywords**】 high altitude heart disease; high altitude pulmonary hypertension; hypobaric and hypoxia; vascular remodeling; pathogenesis; therapy

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慢性高原病(chronic high altitude disease, CHAD)是高海拔地区面临的公共卫生问题之一。CHAD 是指长期生活在高海拔地区(≥2500 m)的居民,对高原环境丧失习服所致的独特临床综合征[1]。CHAD 被分为高原衰退症(high altitude deterioration, HADT)、高原红细胞增多症(high altitude polycythemia, HAPC)、高原心脏病(high altitude heart disease, HAHD)和慢性高山病(chronic mountain sickness, CMS)等 4 种临床分型[2]。其中,HAHD 是因肺动脉压力升高使右心室压力负荷增加,最终导致右心衰竭的一类心血管疾病。在国外,HAHD 被称为“高原肺动脉高压(high altitude pulmonary hypertension, HAPH)”[3]。2022 年欧洲心脏病学会(european society of cardiology, ESC)和欧洲呼吸学会(european respiratory society, ERS)指南将 HAHD 归为肺动脉高压(pulmonary hypertension, PH)第三大类,作为 PH 的一个独立类别[4-5]。HAHD 特点是起病缓慢、持续时间长、早期临床症状不典型和无特异性。由于缺乏临床诊断意识,常发生漏诊或延迟诊断的情况[6]。HAHD 发生发展的主要病理改变为氧化应激、内皮细胞功能障碍以及肺动脉平滑肌细胞(pulmonary artery smooth muscle cells, PASMCs)增殖[7]。由于高海拔地区在气候、个体遗传、生活方式以及人群对不同海拔地区适应和习服过程之间的相互作用复杂多变,这限制了研究人员对高海拔地区居民心血管系统相关健康结局的直接预测[8]。并且近几年对 HAHD 的研究主要聚焦在临床防治,对其机制研究资料较少。因此,深入探讨 HAHD 发病机制及治疗最新研究进展,对 HAHD 预防及临床治疗具有指导意义。

1 高原心脏病流行病学

在世界范围内,因为 CHAD 种族、居住海拔和高海拔祖先生活历史不同,所以其患病率存在差异[9]。尤其是海拔高度对心血管疾病发展的影响非常显著。随着海拔升高,HAHD 发病率增加[8]。HAHD 会影响高海拔暴露人群的肺动脉压以及左右心功能。据估计,HAHD 的全球普遍患病率在 10%~15%之间,其因高原暴露类型而异[3]。例如,在高原居住人群中,约有 6%~12%的个体患病率可高达 36%[10];前往高海拔地区的运动人群,HAHD 患病率约为 4%;在高海拔地区工作的人群,HAHD 患病率约为 9%[11]。此外,高原地区男性 PH 患病率高于女性[12]。心电图结果显示,约有 14%的吉尔吉斯高地居民有右心室肥大的表现[13]。在海拔 4500~4700 m 的高原上,约有 24.9%的居民患有缺氧性右心室肥大,其控制不当会进一步发展为 HAHD[14]。中国藏族居民 HAHD 患病率为 3.2%[15]。这些数据表明 HAHD 是一个值得深入研究的医学问题,其严重影响患者的生活质量,严重威胁患者的生命健康。

2 高原心脏病特点和临床表现

HAHD 是发生于高海拔地区,患者平均肺动脉压(mean pulmonary arterial pressure, mPAP)>30 mmHg,或肺动脉收缩压(pulmonary artery systolic pressure, PASP)>50 mmHg,通常伴有右心室肥大、心力衰竭、中度低氧血症且无过度红细胞增多症的一类 CMS[16]。女性血红蛋白(hemoglobin, Hb)值<19 g/dL,男性 Hb 值<21 g/dL。早期患者无明显症状,剧烈运动时症状变得明显;随着肺动脉压力升高,逐渐出现全身症状。患者最常见的症状是劳力性呼吸困难,随着病情加重,逐渐

出现疲劳、虚弱、头晕、胸痛、雷诺现象、咯血等症状[17]。对患者行体格检查,主要表现于肺血管受累,第二心音明显,反流全收缩期杂音,右心室扩张,可能有右心衰竭发作和全身静脉充血体征[18]。HAHD 患者的心电图结果通常为窦性心动过速、P 波略高尖、aVR 时高 R 波、电轴右偏、顺时针旋转伴 S-T 段正向位移以及 V1 至 V5 导联 T 波倒置;超声心动图显示患者收缩期肺动脉压力升高[19]。

3 高原心脏病发病机制

3.1 低氧引起肺血管收缩和血管重塑

高原低氧应激会引起多种病理变化。血管收缩、肺动脉压力增加、内皮功能障碍、肺泡上皮功能障碍以及炎症反应共同参与 HAHD 病理生理过程[20]。在低氧环境下,许多器官系统利用血管舒张来增加氧气输送。相反,肺对缺氧的应激变化是肺血管收缩增强,血液从氧合不良的肺区向健康的肺泡分流。暴露于缺氧环境几分钟内,肺血管阻力(pulmonary vascular resistance,PVR)和 mPAP 迅速增加,导致肺血管重塑[21]。血管重塑具有不可逆性,消除缺氧刺激后,血管重塑仍持续存在。此外,机体缺氧后缺氧诱导因子-1α(hypoxia inducible factor-1α,HIF-1α)表达上调,促使血管内皮生长因子(vascular endothelial growth factor,VEGF)被合成释放,导致肺血管重塑。研究发现,低氧下转化生长因子-β(transforming growth factor-β,TGF-β)、PINK1/Parkin 通路介导的线粒体自噬以及降钙素基因相关肽(calcitonin gene related peptide,CGRP)也会介导肺血管重塑[22]。

3.2 低氧引起氧化应激和内皮功能障碍

高原低压低氧环境暴露会引发氧化应激,损伤人体多个器官,尤其是大脑和心脏[23]。氧化应激包括活性氧(reactive oxygen species,ROS)产生增加或抗氧化系统耗竭,这两种情况下会引起抗氧化剂和促氧化剂之间的不平衡,ROS 攻击生物膜中的多不饱和脂肪酸,引发脂质过氧化链反应,导致生物膜功能障碍和膜内相关酶的损伤[24-25]。高水平的 ROS 还会引起线粒体损伤、DNA 修饰、细胞因子产生增加,甚至导致细胞死亡[26]。研究发现,急性低压低氧暴露会引起线粒体 DNA 复合体 I 亚基突变,使线粒体呼吸链功能障碍,引起氧化应激反应[27]。研究低氧暴露下大鼠肺动脉变化发现,氧化应激生物标志物和氧化应激相关蛋白,如 NADPH 氧化酶 2(NADPH-oxidase 2,Nox2)和 NADPH 氧化酶 4(NADPH-oxidase 4,Nox4)在大鼠组织中表达增加,超氧化物歧化酶(superoxide dismutase,SOD)和谷胱甘肽过氧化物酶(glutathione peroxidase,GSH-PX)活性降低,这些指标均反映了氧化应激即将增加[28]。此外,长期低氧暴露,内源性舒张因子 NO 合成减少,非对称性二甲基精氨酸增加,这会导致内皮功能障碍,增加 HAHD 患病风险。研究和比较不同亚群结果表明,肺内皮细胞 NO 浓度升高可降低 HAHD 患病率,中国藏族人群体内 NO 浓度较高,所以其 HAHD 患病率较低[29]。因此,暴露于低压低氧环境下,无论何种类型,诱发氧化应激和内皮功能障碍,都会促进高原相关疾病的发生。

3.3 低氧引起心脏损害

长期暴露于高原低氧环境,心血管系统为了满足机体对氧的需求而会发生代偿性改变。机体过度缺氧时会造成水钠潴留,使心脏负荷加重,进一步加速心脏重塑。研究表明,低氧暴露下心率(heart rate,HR)会显著增加[30]。在高海拔地区进行中度运动时,HR 会增加;增大运动强度,HR 会因运动强度增加而加快;但在高原,人的最大运动心率会降低[31]。UDJUS 等[32]研究表明,低氧可引起 HPV,引发右心室重塑。除此之外,长期低氧暴露会影响左室收缩功能,显著降低左心室收缩功能的重要指标:左室射血分数(left ventricular ejection fractions,LVEF)和左室短轴缩短率(left ventricular fraction shortening,LVFS)[33]。参见图 1。

4 高原心脏病治疗

4.1 药物治疗

4.1.1 西药治疗

目前治疗 HAHD 的西药主要包括血管紧张素受体拮抗剂(angiotensin II receptor blockers,ARB)[34]、5 型磷酸二酯酶抑制剂(phosphodiesterase-5 inhibitor,PDE5i)[35-36]、内皮素受体拮抗剂(endothelin receptor antagonist,ERA)[15]、糖皮质激素(glucocorticoid,GC)[37]以

及 NO[38]。厄贝沙坦可以改善血管收缩和炎症反应,逆转肠道菌群丰度[34]。西地那非和他达那非均属于 PDE5i,可通过环磷酸腺苷(cyclic adenosine monophosphate,cAMP)发挥作用,增强红细胞变形能力,减轻血管收缩,进一步扩张血管,减少炎症,目前已被批准用于治疗 HAHD[35-36]。NO 作为一种独特的信号分子和强效血管扩张剂,已经成为新生儿持续肺动脉高压(persistent pulmonary hypertension of newborn,PPHN)的一种新型治疗方法[38]。此外,乙酰唑胺在远隔缺血预处理(remote ischemic preconditioning,RIPC)的辅助下,协同调节血小板源性生长因子 AB 二聚体(Platelet-derived growth factor AB,PDGF-AB),可增强其药效[39]。这些药物主要集中于逆转异常的动脉重塑,虽然有效改善了患者的生活质量,但 5 年病死率仍高达 50%[40]。由于缺氧后动脉重塑涉及多种机制,所以这些药物不足以完全逆转血管重塑和预防右心功能障碍,并且西药存在较大的副作用。因此,开发更有效的治疗 HAHD 方案仍然是未来发展的关键(表 1)。

4.1.2 天然药物治疗

天然药物具有多种药理学特性,成本低,常用来治疗多种疾病。传统的中医、藏医还有几千年来极具特色的草药疗法正在获得高原病领域的关注。目前治疗 HAHD 的天然药物效果较好的有红景天[41-42]、三味檀香散[43]、八味沉香丸[1]、刺五加皂甙 B[44]、千里光[41]以及林柏水提物[45]等。红景天是西藏著名的天然药物,其提取物可恢复缺氧条件下心肌细胞内皮型一氧化氮合酶(endothelial nitric oxide synthase,eNOS)的磷酸化。研究发现,红景天提取物能抑制血管平滑肌增厚和肺血管重塑。其乙酰唑胺联合使用可抑制 HIF-1α 表达,和单独用药相比联合用药时效果更明显[41-42]。三味檀香散是一种传统的藏药,其通过上调 AKT/eNOS/NO 信号通路减轻肺小动

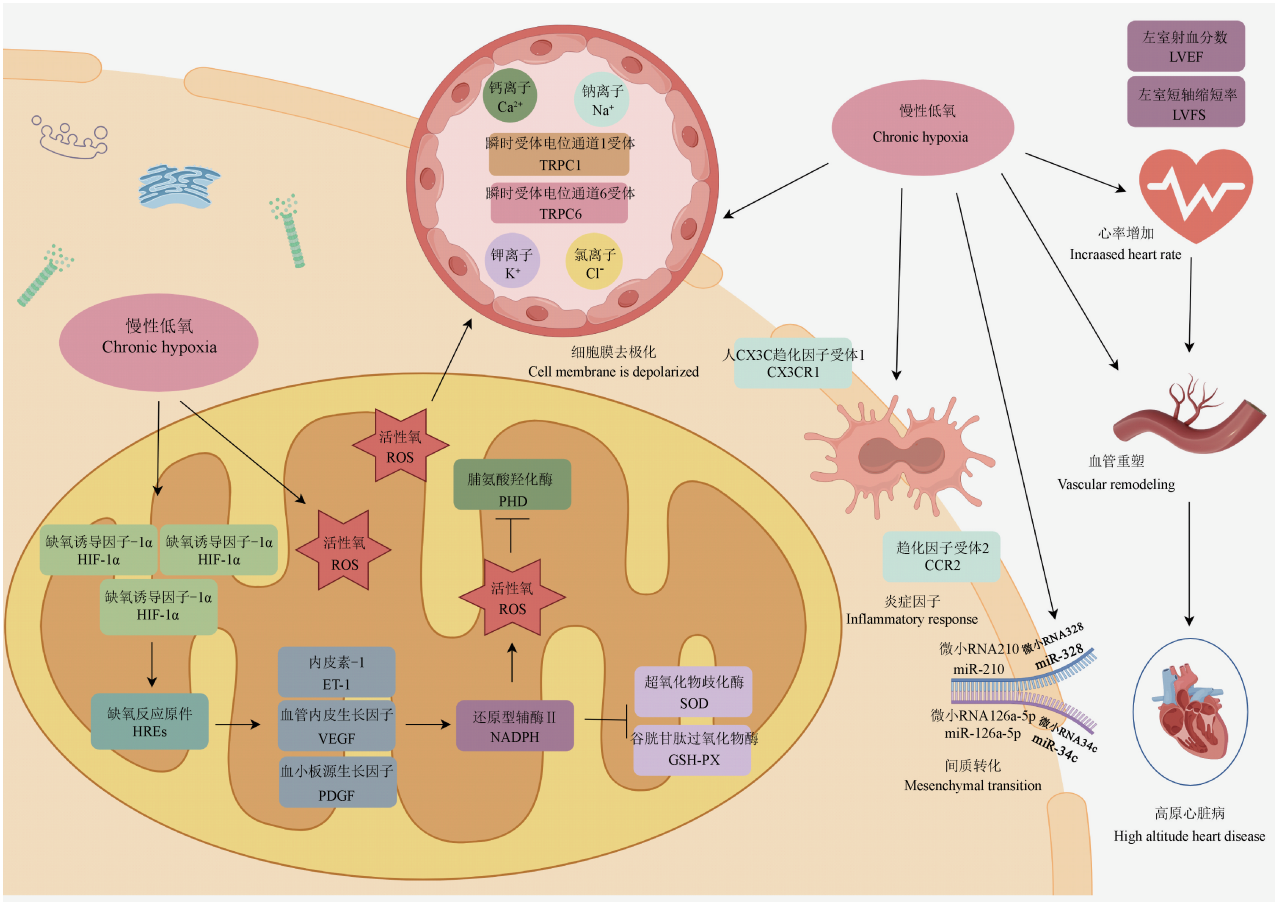

图 1 慢性低氧引起高原心脏病发病机制示意图

Figure 1 Schematic diagram of the pathogenesis of high altitude heart disease caused by chronic hypoxia

表 1 治疗高原心脏病常见西药

Table 1 Western medicines are commonly used to treat high altitude heart disease

药物 Drugs	生物学指标 Biological indicators	模型 Model	作用结果 Action results
波生坦[15] Bosentan	NO、ICAM-1、NF-κB、ET-1	低氧-猪 Hypoxia-pig 低氧-大鼠 Hypoxia-rat	肺动脉高压降低,减少白细胞介导的损伤 Pulmonary hypertension is reduced and leukocyte-mediated damage is reduced
厄贝沙坦[38] Irbesartan	Ang Ⅱ、ET-1、IL-6、NO	低氧-大鼠 Hypoxia-rat	减轻缺氧引起的氧化损伤,降低血管收缩因子和炎症介质的释放 It alleviates oxidative damage caused by hypoxia and reduces the release of vasoconstrictor factors and inflammatory mediators
西地那非[40-41] Sildenafil	NOS、cGMP、PKG、K^+、Ca^{2+}	野百合碱-大鼠 MCT-rat 低氧-大鼠 Hypoxia-rat	模型大鼠血流动力学改善,平均肺动脉压降低 Hemodynamics of the model rats were improved and the mean pulmonary artery pressure was decreased
他达那非[41] Tadalafil	NOS、cGMP、sGC	野百合碱-大鼠 MCT-rat 低氧-大鼠 Hypoxia-rat	有效抑制模型大鼠的肺动脉重塑 It can effectively inhibit pulmonary artery remodeling in model rats
曲前列尼尔[42] Treprostone Neil	EP2、EP4、PPAR	野百合碱-大鼠 MCT-rat 低氧-大鼠 Hypoxia-rat	血管收缩改善,肺动脉压力降低 Vasoconstriction improved and pulmonary artery pressure decreased
乙酰唑胺[42] Acetazolamide	NO、cGMP、NOS、Ca^{2+}	低氧-大鼠 Hypoxia-rat	模型大鼠血流动力学改变,逆转血管重塑 Hemodynamic changes in the model rats reversed vascular remodeling
地塞米松[43] Dexamethasone	NF-κB、Na^+、HIF-1α、IL-1β	低氧-猪 Hypoxia-pig 低氧-大鼠 Hypoxia-rat	降低肺血管阻力,氧合能力改善 Pulmonary vascular resistance was reduced and oxygenation was improved
贝前列素[44] Beraprost	K^+、Ca^{2+}、ATP、PGI2、cAMP、PKA	低氧-大鼠 Hypoxia-rat	降低平均肺动脉压,逆转模型大鼠肺动脉重塑 Mean pulmonary artery pressure was reduced to reverse pulmonary artery remodeling in the model rats

注:ICAM-1:细胞间黏附分子-1;NF-κB:核因子 κB;cGMP:环磷酸鸟苷;PKG:cGMP 依赖蛋白激酶 G;sGC:可溶性鸟苷酸环化酶;EP2:前列腺素 E 受体 2;EP4:前列腺素 E 受体 4;PPAR:过氧化物酶体增殖物激活受体;IL-1β:白介素-1β;PKA:蛋白激酶 A。

Note. ICAM-1, Intercellular adhesion molecule-1. NF-κB, Nuclear factor kappa B. PKG, Protein kinase G. sGC, Soluble guanylate cyclase. EP2, Prostaglandin E receptor 2. EP4, Prostaglandin E receptor 4. PPAR, Peroxisome proliferator-activated receptors. IL-1β, Interleukin-1β. PKA, Protein kinase A.

脉血管重塑,进一步改善 HAHD[43]。八味沉香丸通过改善糖和脂肪酸代谢紊乱,可减轻 HAHD 患者右心室肥厚[1]。随着现代药理学和分子生物学技术的不断进步,更多天然药物将被用于临床治疗,这为 HAHD 患者带来了新的希望(表 2)。

4.2 非药物治疗

4.2.1 间歇复氧和心理治疗

目前治疗 HAHD 的首选方法是增加氧供,解除个体低氧状态。在航空生理学中,基于生理等效高度的供氧是预防缺氧影响的主要方式之一。根据这一原理,在 5000 m 吸入氧浓度为 42%时,生理等效海拔约为海平面,大鼠在低压氧仓中生存 2 周不会出现生长抑制或心血管功能障碍[46]。但是对于高海拔地区来说,5000 m 的高度始终保持吸入氧浓度为 42%不太现实,所以研究人员提出间歇复氧的方法。间歇复氧的频率和总时间需要严格把控,例如在缺氧大鼠模型中间歇 3 h/d 复氧能有效改善低氧所致的肺动脉压力升高[47]。间歇复氧对 ROS 和线粒体的影响不同,线粒体靶向抗氧化作用可以增强间歇复氧的保护作用[7]。

表 2 治疗高原心脏病常见天然药物

Table 2 Common natural medicines for high altitude heart disease

药物 Drugs	生物学指标 Biological indicators	模型 Models	作用结果 Action results
复方丹参滴丸[3] Compound Danshen dripping pills	HIF-1α、PI3K、AKT	低氧-大鼠 Hypoxia-rat	复方丹参滴丸挽救了缺氧状态下心脏和心肌细胞的损伤 Compound Danshen dripping pills rescued the damage of heart and myocardial cells under hypoxia
芍药苷[6] Paeoniflorin	FDX1、DLAT、ROS	低氧-大鼠 Hypoxia-rat	减轻炎症、细胞凋亡和心肌纤维化 Reduce inflammation, apoptosis and myocardial fibrosis
芜菁[6] Turnip	PI3K、AKT、mTOR	低氧-大鼠 Hypoxia-rat	提高对缺氧的耐受性,增加红细胞的携氧能力 It improves the tolerance to hypoxia and increases the oxygen carrying capacity of red blood cells
鼠尾草[13] *Salvia japonica* Thunb	Khk、AldoB、CyclinD1、HIF-1α	野百合碱-大鼠 MCT-rat 低氧-大鼠 Hypoxia-rat	抑制氧化还原并能抑制果糖代谢 It inhibits REDOX and can inhibit fructose metabolism
黄芩苷[46] Baicalin	PI3K、CXCR4、AKT、HIF-1α	低氧-大鼠 Hypoxia-rat	有效抑制肺动脉平滑肌细胞的增殖、迁移和表型转化 It effectively inhibited the proliferation, migration and phenotypic transformation of PASMCs
红景天[46-47] Rhodiola rosea	AhR、NF-κB、Nrf2、HO-1、K^+	野百合碱-大鼠 MCT-rat 低氧-大鼠 Hypoxia-rat	降低模型大鼠平均肺动脉压,逆转低氧诱导的肺动脉平滑肌细胞增殖 Mean pulmonary artery pressure of the model rats was reduced, and the proliferation of PASMCs induced by hypoxia was reversed
三味檀香散[48] Three flavors sandalwood powder	ROCK 1、ROCK 2、NFATc3	低氧-大鼠 Hypoxia-rat	改善模型大鼠心肌缺血,左心室收缩和舒张功能 Improved myocardial ischemia, left ventricular systolic and diastolic function in the model rats
刺五加皂甙 B[49] Eleutheroside B	Nrf2、ROS、RIPK1、RIPK3、NF-κB	低氧-大鼠 Hypoxia-rat	减轻氧化应激,减少铁死亡和坏死性凋亡 It also alleviated oxidative stress and reduced ferroptosis and necroptosis
八味沉香丸[4,50] BaWei ChenXiang Wan	SOD、GSH-PX、NO、NOS	低氧-大鼠 Hypoxia-rat	改善葡萄糖和脂肪酸代谢紊乱,减轻模型大鼠右心室肥厚 Improve glucose and fatty acid metabolism disorders, reduce right ventricular hypertrophy in model rats

注:PI3K:磷脂酰肌醇-3-羟激酶;FDX1:铁氧还蛋白 1;DLAT:二氢硫辛酰胺转乙酰基酶;mTOR:哺乳动物雷帕霉素靶蛋白;Khk:果糖激酶;AldoB:果糖二磷酸醛缩酶 B;CXCR4:趋化因子全长受体蛋白;AhR:芳烃受体;Nrf2:核转录因子红系 2 相关因子 2;HO-1:血红素加氧酶 1;ROCK 1:Rho 激酶 1;ROCK 2:Rho 激酶 2;NFATc3:钙调磷酸酶依赖 3;RIPK1:受体相互作用蛋白激酶 1。

Note. PI3K, Phosphatidylinositol-3-hydroxykinase. FDX1, Ferredoxin 1. DLAT, Dihydrolipoamide transacetylase. mTOR, Mammalian target of rapamycin. Khk, Fructose kinase. AldoB, Fructose-bisphosphate aldolase B. CXCR4, C-X-C chemokine receptor type 4. AhR, Aryl hydrocarbon receptor. Nrf2, Nuclear factor-erythroid 2-related factor-2. HO-1, Heme oxygenase-1. ROCK 1, Rho associated coiled-coil forming protein kinase 1. ROCK 2, Rho associated coiled-coil forming protein kinase 2. NFATc3, Calcium dependent phosphatase 3. RIPK1, Receptor-interacting protein kinase 1.

此外,高原习服需要协同作用,不同的身体系统在个体遗传、表观遗传和心理测量等方面均有差异。大量证据表明,身体和心理之间存在相互关系,在生理健康,但心理存在风险的情况下,其患病风险会增高[51-52]。对 HAHD 患者进行只进行病理治疗是不够的,还需要研究确定与适应该病症生活有关的潜在心理机制[53]。当前流行的“双心医学”突破了传统医学模式,逐步向医学与心理相结合的模式进军。在治疗患者疾病的同时,医者不再只关注疾病本身,也会注重患者

的心理问题,这使得疾病的治疗效果大大提升。

4.2.2 干细胞和肺移植治疗

干细胞是一种未分化,不成熟的细胞,其具有高度分化,自我增殖的潜力,可以再生为各种器官和组织细胞[48]。内皮祖细胞(endothelial progenitor cells, EPCs)和多能干细胞(inducedpluripotent stemcells, iPSCs)是最常见的用于治疗 PH 的干细胞类型。PH 患者 EPCs 水平普遍较低,向患者体内输注 EPCs 可以逆转其肺动脉压力升高,恢复抗炎菌群水平,改善免疫调节功能性微生物群,从而治疗 HAHD[49-50,54-55]。iPSCs 通常被用于 PH 的各种细胞模型[56]。细胞输注疗法既简单又直接,得到了许多医生的广泛认可。

对于重度 HAHD 患者或晚期 HAHD 患者来说,药物和干细胞疗法效果不显著,肺移植是挽救其生命的最佳治疗选择。由于患者单侧肺移植可能发生感染、排斥反应以及原发性移植物功能障碍,所以关于选择肺移植候选者的共同声明支持将双侧肺移植作为 HAHD 的主要治疗手段[57]。但移植术后,患者心输出量减少,左心室长期充盈不足,其需要预防性延长体外膜肺氧合(extracorporeal membrane oxygenation, ECMO)的使用时间[58]。

5 高原心脏病研究现有特点及不足

医学在进步,高原医学获得了越来越多的关注。研究人员对 HAHD 发病机制和治疗的研究也日渐深入。HAHD 发病机制:缺氧引起 HPV 导致肺血管重塑;内皮源性舒张因子分泌异常,导致内皮功能障碍;离子通道改变导致肺动脉压力升高;氧化应激加剧以及表观遗传改变等。但仍有许多致病基因尚未被发现,许多表观通路仍需要探索。HAHD 治疗方面:目前 HAHD 有效的靶向药物治疗以单药或联合用药为主。基于 ERA、PDE5i 和 PCAs 途径的新型口服药物已被引入 HAHD 常规治疗范畴,但西药存在一定的副作用。对此天然药物治疗 HAHD 成为热门话题。非药物治疗上,干细胞疗法效果很显著,但其有潜在的致癌风险。研究显示,受体动物患癌症的风险高于正常动物[59]。充分评估干细胞潜在风险至关重要。肺移植对重度患者效果明显,但其存在一定的排异反应,也需充分评估风险。因此,对 HAHD 机制的研究需要更加深入,其治疗方案也需要更加优化。

6 总结与展望

总之,HAHD 是一种由于高原环境引起的低氧血症而发生的疾病暴露。随着西部开发和旅游业的发展,前往高原工作、休闲的人越来越多,科研人员对 HAHD 机制方面研究不断深入,期望发现更多治疗 HAHD 的途径。结合基础科研成果,治疗方面不断优化治疗方案,采用中西联合用药的方案,凸显了将研究数据从实验室到床旁并最终到患者的无缝转化的重要性。然而,HAHD 发病率仍然很高,这表明该领域在治疗方面仍需要创新和改善。希望在未来几十年里,将有更多的数据填补现有的知识盲区,可以为患者找到更好的治疗方案。

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进展快报

膝关节骨性关节炎:动物模型及中药干预研究进展

膝关节骨关节炎(KOA),也称为退行性关节炎,是一种基于退行性病理改变的疾病,其特征是骨增生、滑膜炎性病变、软骨变性和底层骨硬化。近年来,KOA 的发病率和致残率逐年上升,严重影响了患者的生活质量。针对 KOA 的研究不仅集中在发病机制和临床治疗中,还涉及到动物模型的构建及中药干预的效果评估。

KOA 的动物模型是研究该疾病发病机制和筛选治疗药物的重要工具。常用的动物模型包括兔子、大鼠和小鼠等,这些模型通过外科手术、化学药物诱导或遗传操作来模拟人类 KOA 的病理特征。中药作为 KOA 治疗中的一部分,因其多靶点、少副作用的特点,受到越来越多的关注。研究表明,多种中药及其复方在动物模型中表现出显著的抗炎、镇痛和软骨保护作用。黄芪、杜仲等中药可以通过调节炎症因子和细胞信号通路,减缓软骨的退化。此外,一些复方制剂如独活寄生汤和芍药甘草汤也在动物实验中显示出良好的治疗效果。

山东大学高等医学研究院、第二医院孙蓉教授领衔的研究团队依托国家中医药管理局高水平重点学科,对 KOA 的动物模型及中药干预的研究进展进行探讨,旨在为相关领域的研究提供参考。

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