

氢分子对心肌损伤的防护效应及机制*

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摘要 近年来, 氢分子的生物医学效应引起广泛关注. 氢分子极小, 且具有高扩散性, 不仅能透过血脑屏障, 还能穿过各种细胞膜进入胞浆、线粒体、细胞核和内质网等亚细胞结构, 甚至可进入生物大分子内部, 与靶分子发挥作用. 近期研究表明, 氢分子在缓解电离辐射、缺血再灌注、心脏移植、心肺复苏术和心肺转流术等所致心脏损伤中有很好的预防和辅助治疗效果, 并且副作用极小. 氢分子作用的机制可能与其抗氧化、抗炎、抗凋亡及调节线粒体代谢相关, 但其确切机制还需更多更深入的研究.

关键词 氢分子, 心脏损伤, 抗氧化, 抗炎, 抗凋亡, 线粒体

学科分类号 R52, Q5

DOI: 10.16476/j.pibb.2015.0032

氢气是一种无色、无味的最轻气体^[1], 在体温条件下能够与生物分子自发进行特异性反应^[2]. 它的高扩散性使其不仅能透过血脑屏障, 还可穿过细胞膜结构进入胞浆、线粒体、细胞核、内质网等亚细胞结构, 与靶分子发生作用^[3-5]. 氢气温和的还原性使其对体内氧化还原平衡及参与信号转导的活性氧(reactive oxygen species, ROS)影响较小^[6]. 临床试验也未见氢气有明显毒副作用^[6].

早在 1888 年, 有医生就用注射器将氢气从肛门注入患者体内, 通过叩诊追踪膨胀部位, 以判断并定位内脏破损^[7]. 此后, 有学者发现吸入高压氢可使皮肤瘤显著退化^[8], 但这一现象并没引起学术界足够重视. 直至 2007 年, 氢气被证明是一种具有治疗和预防作用的抗氧化剂, 通过选择性地减少强氧化剂如羟自由基($\cdot\text{OH}$)和过氧化亚硝酸盐(ONOO^-)而发挥其抗氧化效应, 进而保护细胞免遭氧化损伤^[9], 氢气的生物医学效应才备受关注. 自此, 氢分子研究进入一个崭新时代. 目前的实验研究提示, 氢分子可作为细胞或器官重要的生理调控因子, 起到抗氧化、抗炎、抗凋亡等作用, 进而可能对心脑血管疾病、呼吸道疾病、癌症和代谢综合征等严重危害人类健康的疾病有很好的改善作用^[8].

心脏病是威胁人类生命的重大疾病之一, 据统计, 全世界每年死于心脏病的人数占总死亡数的

1/3, 我国每年有几十万人死于心脏病. 目前已有不少研究表明, 氢气在缓解心脏损伤, 如缺血再灌、电离辐射、心脏移植、心肺复苏、心脏停跳和动脉粥样硬化等损伤中有很好的疗效, 但其保护机制目前还不很明确. 本文旨在综述氢在心脏损伤防护方面的最新研究进展.

1 氢在生物体内的代谢

1.1 内源氢的合成与代谢

一些肠道细菌如大肠杆菌, 通过对大肠内未消化糖类的发酵生产大量分子氢^[10-11]. 利用微电极可在小鼠体内检测到氢, 并发现盲肠内氢含量最高, 其次是小肠、大肠、肝脏、脾脏和血液等组织^[12]. 另有研究发现, 内源氢的含量已明显超出外源氢发挥抗氧化能力的最低浓度, 如肝脏内源氢浓度近乎 $60\ \mu\text{mol/L}$ (而外源氢能达到的有效剂量仅为 $25\ \mu\text{mol/L}$), 但当氧化应激或炎症发生时, 内源氢却不起明显作用^[8].

* 中央高校基本科研业务费专项资金(08143008, 08143101)和陕西省科技攻关项目(2013K12-01-10)资助.

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收稿日期: 2015-05-03, 接受日期: 2015-06-30

有报道称,内源氢是被结肠黏膜或胃中其他共生菌清除,如可消耗大量氢的螺杆菌^[13],而大部分哺乳动物缺乏异化酶,不能将细菌代谢物重新利用以生产氢。也有数据表明,肠道细菌发酵产生的氢不能被宿主利用,多数是随粪便、肠胀气排出或被甲烷杆菌吸收,少数随血液流动,随后经肺排出^[6]。有学者称,对机体进行抗菌治疗也许能改变肠道共生菌数量,以从根本上提高内源氢产量,进而增强机体自身抗氧化能力。也可通过一些食物和药物,如棉籽糖、乳糖、山梨醇、甘露醇、姜黄等来促进内源氢的产生^[6]。研究内源氢的合成与代谢对进一步挖掘氢分子生物医学效应有深刻意义,值得深入探讨。

1.2 外源氢的摄入与代谢

常见的外源氢摄入方法有直接吸入氢气、口服富氢水及注射富氢生理盐水^[6]。对新西兰大白兔分别进行等氢气含量的氢气腹腔注射、富氢生理盐水腹腔注射及静脉注射,发现不同给氢方式下兔的氢气代谢不同。腹腔注射氢气能更长时间维持呼气氢气保持在较高浓度状态^[14];与注射富氢水相比,腹腔注射氢气不会影响机体液体负荷,更安全便捷。但对于何种给氢方式具有更好的疗效,仍有待进一步研究^[14]。

机体吸入氢气时动、静脉的氢气浓度不同,且氢气可进入组织中^[9]。假定氢分子的泄露、皮肤表面的散发、结肠菌体对氢气的消耗可忽略不计,通过同步测量摄入富氢水前后的换气量和呼出氢气体量,可准确测定摄入富氢水后氢分子在机体内的消耗。在摄入富氢水前,呼出氢气体积分数的平均基线为 $(6.9 \pm 0.7) \times 10^{-6}$ 。摄入富氢水后,受试者呼出氢气体量呈先迅速增加后逐渐降低的趋势,于摄入后 10 min 达到最大值 $(35.6 \pm 12.3) \times 10^{-6}$,60 min 时降到基线水平^[15]。摄入体内的氢气 60% 散失,约 40% 被人体消耗,且氢的消耗量可能与体内氧自由基的含量密切相关^[15]。

2 氢分子对不同类型心脏损伤的防护

2.1 对电离辐射的防护

电离辐射可导致慢性心功能受损和心脏病^[16],最明显的是诱发心肌毛细血管内皮碱性磷酸酶活性丧失而使心肌受损^[17-18],进而导致心肌退化^[19]。已知电离辐射造成的心脏损伤与 ROS 密切相关^[20], $\bullet\text{OH}$ 是活性极高的 ROS,易于造成细胞及组织氧化损伤,氢分子可选择性清除 $\bullet\text{OH}$ ^[9]。如用富氢磷

酸盐缓冲液(phosphate buffered saline, PBS)预处理细胞,可提升细胞对辐射的耐受能力^[21]。小鼠在辐照前给予富氢水干预(0.6 mmol/L 富氢水)处理小鼠 33 d,在停止辐照后第 13 d,与未处理组相比,富氢水预处理组小鼠存活率有极显著提高,心肌细胞的丙二醛(malondialdehyde, MDA)和 8 羟基脱氧鸟苷(8-hydroxy-2'-deoxyguanosine, 8-OHdG)水平明显降低,总超氧化物歧化酶(superoxide dismutase, SOD)和谷胱甘肽(glutathione, GSH)显著升高。这表明氢分子可通过增强心肌细胞自身的抗氧化能力而减小因辐照对心肌等组织的氧化损伤,提高小鼠存活率^[21]。

有学者设想,给宇航员吸氢或口服富氢水也许能预防宇宙辐射^[22]。氢分子有可能作为一种有效的辐射防护剂用于心脏保护,遗憾的是辐射防护机制尚不清楚,临床试验还较少^[23-24]。

2.2 对心脏缺血再灌注损伤的缓解

心脏是最可能发生缺血再灌注的组织之一。心脏的缺血再灌注会造成一些损伤,如再灌注性心律失常、心肌顿抑和急性心肌梗死。在急性心梗模型中,从缺血开始到再灌注后 60 min 期间给大鼠通入氢气,能有效减小梗塞面积,增强左心室功能恢复^[25]。富氢生理盐水可降低促炎性细胞因子和黏附分子(intercellular cell adhesion molecule-1, ICAM-1)的水平,从而抑制大鼠心脏缺血再灌注引起的炎症反应^[26]。对小猎犬的冠状动脉左前降支堵塞 90 min 后再灌注 6 h,在灌注前 10 min 到灌注 1 h 期间对其通入 1.3% 氢气,再灌注造成的心肌梗塞可被有效缓解,但这种缓解并不依赖氢气的抗氧化功能或 NADH 脱氢酶通路,而是通过开放 mKATP (mitochondrial ATP-sensitive K^+ channels) 后抑制 mPTP (mitochondrial permeability transition pores) 来起作用^[27]。另有发现,在灌注前 1 h 到灌注后 1 h 间,单独用氢气(1%~3%)或氢气与一氧化碳(体积分数 $50 \times 10^{-6} \sim 250 \times 10^{-6}$)混合气体可有效减少再灌注大鼠心肌梗塞面积、钙蛋白 I 及磷酸肌酸激酶(creatine phosphate kinase, CPK)的含量,继而改善心脏缺血再灌注损伤^[28]。富氢生理盐水也能显著降低再灌注大鼠心肌梗塞面积、易损区 MDA 浓度、8-OHdG 及含半胱氨酸的天冬氨酸蛋白水解酶 3 (cysteinyl aspartate specific proteinase3, caspase-3)水平,进而缓解心肌损伤^[29]。诸多研究提示,摄入氢分子可能成为临床冠状动脉手术方便、安全又经济的辅助治疗手段。

2.3 对心脏移植损伤和血管病变的控制

氧化应激可导致移植血管病变和间质纤维化, 从而限制心脏移植后个体的长期存活. 从心脏移植开始, 连续 100 d 给大鼠摄入富氢水, 可显著降低移植引起的心脏组织炎性细胞浸润、脂质过氧化程度以及干扰素 γ (interferon, $\text{IFN}\gamma$) 水平, 延长心脏移植大鼠的寿命^[30]. 在 4℃ 下对移植前的离体大鼠心脏用不同氢气含量的组氨酸 - 色氨酸 - 酮戊二酸 (HTK) 保存 6 h 后进行再灌注, 发现富氢组心肌细胞的 8-OHdG 及 MDA 水平降低, SOD 活性被维持, 肿瘤坏死因子 α (tumor necrosis factor α , $\text{TNF-}\alpha$) 及白介素 6 (interleukin-6, IL-6) 水平下降、凋亡相关基因 Bax (Bcl-2 associated X protein) 及 caspase-3 活性降低, 而 B 淋巴细胞瘤 2 蛋白 (B-cell lymphoma-2, Bcl-2) 的 mRNA 及蛋白质水平都被上调, 且氢分子的保护效应存在剂量依赖性^[31]. 富氢水干预可明显抑制移植心脏主动脉内膜增生、T 细胞增殖、白介素 2 (Interleukin-6, IL-2) 及 $\text{IFN}\gamma$ 水平升高, 也增加了移植心脏 ATP 生成水平及线粒体呼吸链相关酶的活性, 显著延长了心脏移植后移植体的存活时间^[32].

上述研究结果提示: 氢分子可通过抑制心脏完全缺血引起的氧化应激、炎症因子及凋亡因子而延长心脏可缺血时间, 可用于对即将移植心脏的离体保存; 富氢水可成为治疗急性排斥反应的潜在药物, 通过抑制炎症相关反应及维持线粒体活力来减弱心脏移植损伤, 用于心脏移植的辅助治疗.

2.4 对心肺转流术损伤的缓解

心肺转流术即利用体外循环设备, 为患者提供充足氧气并保证重要脏器血流, 维持患者生命的临床手段^[33-34]. 然而心肺转流术造成的心脏损伤会伴随机体炎症反应, 进而明显增加心肺转流术期间的死亡率和并发症的发生率^[35-37]. 研究证明, 在大鼠心肺转流术期间吸氢 60 min 可明显抑制炎症反应^[38], 是缓解手术并发症的有效手段.

2.5 对高脂饮食所致心脏损伤的防治

高脂饮食可对心脏造成损害, 主要表现为心脏肥大、心肌僵硬、心脏收缩功能紊乱, 进而引起心脏重塑, 引发心脏病^[39-40]. 健康受试人群在进行 5 d 高脂饮食后, 心脏高能磷酸盐代谢受损, 磷酸肌酸 /ATP (phosphocreatine /ATP, PCr/ATP) 降低^[41]. 高脂饮食大鼠出现心肌纤维化、间隙胶原沉积, 心肌细胞 IL-6、 $\text{TNF-}\alpha$ 、单核细胞趋化蛋白 1 (monocyte chemotactic protein 1, MCP-1) 及 ICAM-1

水平增加, 心脏匀浆中依赖于 NADH 的超氧化物产量显著升高^[42]. 对高脂饮食所致的心脏代谢受损人群每天摄入富氢水 1.5~2 L, 持续 8 周, 发现受试者脂质过氧化、DNA 损伤程度显著下降、SOD 水平显著升高^[6]. 此结果提示, 富氢水可成为一种新型治疗剂, 用于防治高脂饮食所致的心肌代谢受损.

2.6 对心肺复苏的保护作用

心脏骤停严重威胁人类的生命. 对心脏骤停大鼠在开始心肺复苏术 (cardiopulmonary resuscitation, CPR) 到恢复自主循环 (restoration of spontaneous circulation, ROSC) 2 h 期间通入高氧 (98%) 及 2% 氢气, 并结合温度控制, 发现 37℃ 吸氢可抑制左心室舒张期末压升高、抑制 8-OHdG 和 4-羟基壬烯醛 (4-hydroxynonenal, 4-HNE) 水平并增加 IL-6 水平, 且吸氢比低温治疗在改善大鼠存活及神经功能缺损程度 (neurological deficit score, NDS) 方面更有效^[43]. 对心脏骤停大鼠在 ROSC 开始后的 2 h 期间通入氧 (26%) 及 1.3% 氢气, 可显著提高大鼠复苏 7 d 后的存活率, 并有效抑制大脑易损区神经元退化及小神经胶质细胞活性^[44]. 对健康成年大鼠进行 8 min 窒息使其心脏骤停, 并分别于心肺复苏术前 1 min、ROSC 后 6 h 及 12 h 对其分别注射不同剂量的富氢生理盐水, 发现富氢生理盐水可剂量依赖性地提高大鼠存活及神经功能; 也可改善脑损伤, 体现在海马 CA1 区神经元数目增加、大脑皮层及海马水肿程度降低, 并且维护了血脑屏障的完整性; 降低了血清中 S100B (soluble protein-100B) 水平及神经特异性烯醇化酶活性; 降低了氧化产物 8-异前列腺素 $\text{F}_{2\alpha}$ (8-iso-prostaglandin $\text{F}_{2\alpha}$, 8-iso-PGF $_{2\alpha}$) 和 MDA 水平, 降低了 $\text{TNF-}\alpha$ 及白介素 1 β (interleukin-1 β , IL-1 β) 水平, 增加了血清和脑组织中抗氧化酶 SOD 和过氧化氢酶活性, 还降低了大脑皮层及海马区 caspase-3 活性^[45]. 对心脏骤停兔子在心肺复苏术期间腹腔注射氢气, 可提高复苏后 72 h 的存活率, 改善神经功能缺损程度、减少神经元损伤并抑制其凋亡、降低血浆和海马组织氧化应激并增强抗氧化酶活性, 但不同氢气剂量间无明显差异^[46]. 由此可见, 吸氢可缓解心脏骤停对心、脑的损害并降低死亡率.

目前关于氢分子对心肺复苏的保护效应研究, 主要表现在探索给氢方式及给氢含量、氢分子对复苏后 1~7 d 的存活率、NDS、舒张压等的改善, 较少涉及氢分子对心肌组织内部生化指标, 如氧化

应激、炎症、凋亡等相关指标的影响,对氢分子作用机理的探讨则更少.而存活率、NDS一定与这些指标水平的改变紧密相关.因此,探究心肌组织生化指标的改变,也许是阐明氢分子对心脏保护机理的重要途径.由此,吸氢作为心肺复苏术的辅助治疗手段也将成为可能.

2.7 在其他心脏损伤模型中的应用

此外,氢分子在其他疾病中的心脏损伤防治作用也在不断被发现.例如,对野百合碱诱导的肺动脉高血压大鼠用氢气处理 14 d 后,肺动脉高压引起的右心室肥大被明显抑制^[47].对用广谱抗癌药物顺铂处理过的小鼠给予吸氢或口服富氢水处理,可有效改善由顺铂引起的氧化应激对肾脏的毒副作用,并且不影响顺铂的抗癌疗效^[48].而被广泛应用的抗癌药物阿霉素对心肌有严重毒副作用,并也证实这种毒性与氧化应激有关^[49-50].由此推测,氢分子干预也许能缓解一些抗癌药物如阿霉素等对心肌的毒性,从而作为癌症病人化疗的辅助手段.

3 氢分子心脏损伤防治作用的可能机制

3.1 抗氧化机制

氢分子的抗氧化功能表现为对 ROS 的直接清除能力^[25].氢可有效清除心脏损伤产生的 $\cdot\text{OH}$,并能增强机体自身抗氧化能力,如提高 SOD、过氧化氢酶活性和 GSH 水平,进而促进机体对其他 ROS,如超氧阴离子($\cdot\text{O}_2^-$)和过氧化氢(H_2O_2)的清除^[51-52].ROS 可通过上调 NF- κB 信号通路激活 TNF- α 的表达^[53],而 TNF- α 又能激活 NADPH 氧化酶(NOX)的表达,这一过程又会产生 ROS^[54].氢分子又可通过抑制 NF- κB 的激活来减缓炎症反应^[55],故氢分子的抗氧化和抗炎功能相辅相成.另有研究证实,富氢生理盐水能作为移植供体的储存液,延缓心脏移植供体在体外的氧化损伤^[56].

相比于其他抗氧化剂,氢气能选择性抗氧化,它清除 $\cdot\text{OH}$ 及 ONOO $^-$,但并不影响具有生理功能的其他活性氧成分.氢分子极小,更易于透过血脑屏障及细胞膜结构与靶分子发生作用.此外,氢分子氧化反应终产物为水,对机体副作用较小,内源氢的存在,使氢分子进入机体更具组织兼容性^[57].

3.2 抗炎和抗凋亡机制

氢可通过抑制损伤组织产生的促炎因子及活化的淋巴细胞产生的 TNF- α 和 IFN 而发挥其抗炎作用,也可在巨噬细胞中抑制脂多糖(lipopolysaccharides, Lps)/IFN γ 诱导的 NO 生成,

降低 I 型过敏中的炎症反应^[58].新生低氧缺血大鼠模型中,氢可显著抑制凋亡相关酶 caspase-3 和 caspase-12 的活性^[59].氢分子对炎症反应和细胞凋亡的抑制与 TNF- α /NF- κB 通路、Ras-ERK1/2-MEK (methyl ethyl ketone)1/2 通路和丝氨酸/苏氨酸激酶 (protein kinase B, Akt) 通路的激活密切相关^[60-62].已经证实氢气对丝裂原活化蛋白激酶 (mitogen-activated protein kinases, MAPKs) 信号通路中重要的细胞外调节蛋白激酶 (extracellular regulated protein kinases, ERK)、c-Jun 氨基末端激酶 (c-Jun N-terminal kinase, JNK)、p38 等的活性和 PI3K (phosphatidylinositol 3 kinase)/Akt 活性均有调控作用.而叉头框蛋白 O 亚型 (forkhead box O, FoxO) 是一类与氧化应激、凋亡、增殖密切相关的转录因子,其活性受 MAPKs 和 PI3K/Akt 等多种信号途径调控.有学者推测,氢分子可能通过调控 FoxO 信号途径发挥其抗凋亡等功能^[63](图 1).

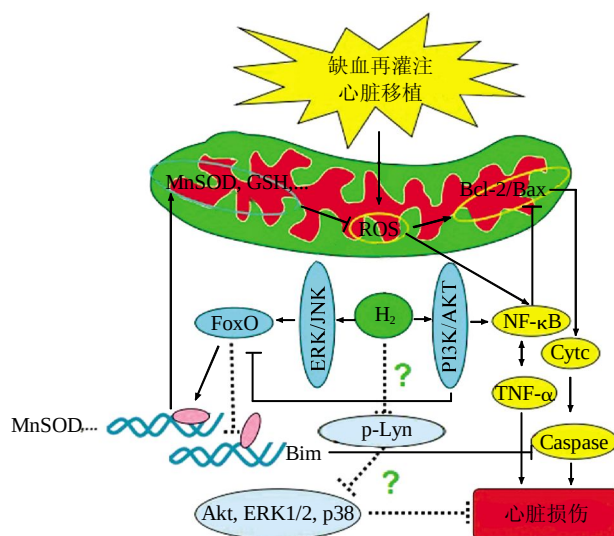


Fig. 1 The possible mechanisms of hydrogen molecular in alleviating cardiac injury and its relationship with mitochondria^[51-66]

图 1 氢分子在心脏损伤防护中的可能机制及其与线粒体的关系^[51-66]

缺血再灌注(ischemia-reperfusion)、心脏移植(heart transplantation)等临床手段会引起线粒体 ROS 产量升高.过量 ROS 不仅引起氧化应激,还可激活 Bax,促使 Cyt c 释放,从而激活 Caspase 级联反应,引起心肌细胞凋亡;过量 ROS 也可激活 NF- κB 通路,引起心肌炎症反应,致心脏受损.氢分子不仅可直接清除部分 ROS;还可通过 ERK/JNK 通路及 PI3K/AKT 通路作用于 FoxO,从而激活 MnSOD 发挥抗氧化功能,可能抑制 bim 发挥抗凋亡作用;也能通过 PI3K/AKT 通路发挥抗炎作用,从而缓解心脏损伤(cardiac injury).氢气也可能作为一种气态信号分子,通过减弱酪氨酸激酶 Lyn 的磷酸化(p-Lyn)而下调 Akt、ERK1/2 和 p38 等下游分子.

3.3 作为一种信号分子

有研究者认为, 氢气可能是继 NO、CO 和 H₂S 之后的第四个气态信号分子^[6]. 氢气通过调控一个特殊信号通路而减弱与免疫球蛋白 E 的高亲和力和受体 FcεRI 有关的酪氨酸激酶 Lyn 的磷酸化, 下调信号转导, 抑制 NADPH 氧化酶活性, 弱化肥大细胞中 Lyn 的磷酸化, 进而它的下游靶分子包括酪氨酸激酶 Syk、磷脂酶 C-γ1 (phospholipase C-γ1, PLCγ1)、PLCγ2、Akt、ERK1/2、p38 和 cPLA2 都被下调^[64]. 要证实这一观点, 还需找到氢气确切的作用靶点及可能存在的受体^[65]. 氢气也可能通过与金属蛋白相互作用而影响信号转导, 因为某些含铁蛋白中铁离子可能成为氢的结合位点^[66] (图 1).

3.4 氢分子与线粒体

上文已提到, 电离辐射、缺血再灌、心脏移植、心肺复苏等对心脏的损伤主要是因产生了 ROS, 引起了心肌细胞氧化应激, 继而引起机体的炎症反应及细胞凋亡. 而线粒体的电子传递链作为细胞能量供应站, 也是 ROS 的发源地^[67-68]. 生物体在进化中已具备有效的抗 ROS 防御体系, 如 SOD、GSH 过氧化物酶(GSH-Px)、维生素 C 等, 但在氧化应激状态下, ROS 水平与机体抗氧化能力失衡, 首先导致线粒体内部的生物大分子, 如抗氧化酶、线粒体复合物、核酸、膜脂等被 ROS 氧化而功能丧失或降低, 进而导致线粒体功能受损, 受损的线粒体会产生更多 ROS, 如此形成恶性循环. Tschopp 等^[69]认为, 线粒体来源的 ROS 是调控 NLRP3 炎症小体的关键信号, ROS 增加会引起炎症反应. ROS 对线粒体膜的损害可破坏线粒体膜电位, 导致线粒体通透性增大, 细胞色素 C 从线粒体膜间隙释放到胞浆, 激活 caspase9、caspase3, 诱导细胞程序性死亡. 骤停心脏复苏后, 线粒体出现 Ca²⁺ 超载、氧化磷酸化受损、细胞色素 C 释放增加^[70]. 由此可见, 线粒体损伤引起的级联反应是电离辐射、缺血再灌注、心肺复苏等临床疗法造成心脏损伤的主要原因.

氢气可进入线粒体. 诸多实验已经证明, 氢分子可缓解电离辐射、心脏移植、心肺复苏等治疗方式对心脏的损伤, 并已初步阐明这种效应的发挥是因氢分子具有抗氧化、抗炎和抗凋亡性能. 虽然具体作用机制还不清楚, 但可以肯定氢分子对心脏的保护效能一定与其对心肌线粒体损伤的防护密不可分. 初步临床试验也表明, 饮用富氢水似乎改善了

线粒体功能紊乱^[71]. 因此, 从线粒体角度入手, 探索氢分子在氧化应激、凋亡、线粒体动态变化及代谢方面的调节机制, 可能是揭示氢分子对心脏损伤防护作用的重要研究思路.

4 展 望

氢分子不仅可有效缓解电离辐射、缺血再灌、心肺复苏、心肺转流术及心脏移植等损伤模型中心脏的损伤, 还可有效预防其他并发症的发生, 且未发现副作用, 具有良好的临床应用优势. 但目前关于氢分子心肌保护作用的机理性研究还较少, 氢分子作用的确切信号通路还未阐明. 线粒体, 可能是氢分子保护效应的靶细胞器, 探究氢分子对线粒体的作用机制也许是探明氢气保护机理的关键, 值得广大学者在此方向继续深入探索.

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The Protective Effects and Mechanisms of Molecular Hydrogen in Cardiac Injury*

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Abstract The biomedical effects of molecular hydrogen have aroused public and academic interest in recent years. Because of its high diffusivity and very small structure, hydrogen has the ability not only to cross the blood brain barrier, but also to infiltrate through the cytomembrane to the cytoplasm, mitochondria, nuclei, endoplasmic reticulum and other subcellular structures, even to interact inner motif of biomacromolecules. It has been proven that hydrogen shows effects on the prevention and treatment of cardiac injury induced by radiation, ischemia-reperfusion, cardiac allografts, cardiopulmonary resuscitation and cardiopulmonary bypass nearly without side effects. These effects have been suggested to be associated with its antioxidant activity, anti-inflammatory effect, anti-apoptosis and role in regulating of mitochondrial metabolism, but further studies are greatly needed for better and deeper understanding of the protective effects of hydrogen in cardiac injury.

Key words hydrogen molecules, cardiac injury, antioxidant, anti-inflammatory, anti-apoptosis, mitochondria

DOI: 10.16476/j.pibb.2015.0032

* This work was supported by grants from The Fundamental Research Funds for the Central Universities (08143008, 08143101), Shanxi Province Science and Technology Research and Development Program (2013K12-01-10).

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Received: May 3, 2015 Accepted: June 30, 2015