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汉黄芩素调节 AMPK/NLRP3 信号通路 对 H/R 诱导的心肌细胞凋亡的影响*

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摘要 目的:探讨汉黄芩素(WOG)调节单磷酸腺苷活化蛋白激酶(AMPK)/NOD样受体蛋白3(NLRP3)信号通路对缺氧/再氧合(H/R)诱导的心肌细胞凋亡的影响。**方法:**将H9C2细胞分为Control组(正常培养)、H/R组(H/R诱导)、L(低剂量)-WOG组、M(中剂量)-WOG组、H(高剂量)-WOG组(在H/R诱导的基础上分别加入40、80、120 $\mu\text{mol/L}$ 的WOG)、WOG+Compound C组(在H-WOG组基础上加入10 $\mu\text{mol/L}$ AMPK抑制剂Compound C)。噻唑蓝(MTT)法和5-乙炔基-2'-脱氧尿嘧啶核苷(EdU)染色检测WOG对H9C2细胞增殖的影响;流式细胞术检测WOG对H9C2细胞凋亡的影响;酶联免疫吸附试验(ELISA)检测H9C2细胞血清氧化应激指标[丙二醛(MDA)、活性氧类物质(ROS)、超氧化物歧化酶(SOD)]和炎症因子[白介素(IL)-1 β 、IL-18]水平;蛋白免疫印迹(WB)法检测H9C2细胞AMPK、NLRP3、B细胞淋巴瘤-2(Bcl-2)、Bcl-2相关X蛋白(Bax)蛋白表达。**结果:**H/R组H9C2细胞的光密度值(OD_{490})、EdU阳性细胞率、SOD、AMPK、Bcl-2低于Control组,细胞凋亡率、IL-1 β 、IL-18、ROS、MDA、NLRP3、Bax高于Control组($P<0.05$);与H/R组比较,L-WOG组、M-WOG组、H-WOG组 OD_{490} 、EdU阳性细胞率、SOD、AMPK、Bcl-2表达升高,细胞凋亡率、IL-1 β 、IL-18、ROS、MDA、NLRP3、Bax降低($P<0.05$);WOG+Compound C组 OD_{490} 、EdU阳性细胞率、SOD、AMPK、Bcl-2低于H-WOG组,细胞凋亡率、IL-1 β 、IL-18、ROS、MDA、NLRP3、Bax表达高于H-WOG组($P<0.05$)。**结论:**WOG可以抑制H/R诱导的心肌细胞凋亡,其机制可能是通过介导AMPK/NLRP3信号通路有关。

关键词:黄芩素;AMPK/NLRP3信号通路;心肌细胞;细胞凋亡

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Effect of Wogonin on H/R Induced Cardiomyocyte Apoptosis by Regulating the AMPK/NLRP3 Signaling Pathway*

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ABSTRACT Objective: To investigate the effect of wogonin (WOG) on hypoxia/reoxygenation (H/R)-induced cardiomyocyte apoptosis by regulating adenosine monophosphate-activated protein kinase (AMPK)/NOD-like receptor protein 3 (NLRP3) signaling pathway. **Methods:** H9C2 cells were divided into Control group (normal culture), H/R group (H/R induction), L (low dose)-WOG group, M (medium dose)-WOG group, H (high dose)-WOG group (40, 80, 120 $\mu\text{mol/L}$ WOG were added on the basis of H/R induction), WOG+Compound C group (10 $\mu\text{mol/L}$ AMPK inhibitor Compound C was added on the basis of H-WOG group). The effect of WOG on the proliferation of H9C2 cells was detected by methyl thiazolyl tetrazolium (MTT) assay and 5-ethynyl-2'-deoxyuridine (EdU) staining. The effect of WOG on apoptosis of H9C2 cells was detected by flow cytometry. The levels of serum oxidative stress indexes [malondialdehyde (MDA), reactive oxygen species (ROS), superoxide dismutase (SOD)] and inflammatory factors [interleukin (IL)-1 β , IL-18] in H9C2 cells were detected by enzyme-linked immunosorbent assay (ELISA). The expression of AMPK, NLRP3, B cell lymphoma-2 (Bcl-2) and Bcl-2 associated X protein (Bax) in H9C2 cells was detected by Western blot (WB). **Results:** The optical density (OD_{490}), EdU positive cell rate, SOD, AMPK and Bcl-2 of H9C2 cells in H/R group were lower than those in Control group, and the apoptosis rate, IL-1 β , IL-18, ROS, MDA, NLRP3 and Bax were higher than those in Control group ($P<0.05$). Compared with H/R group, OD_{490} , EdU positive cell rate, SOD, AMPK and Bcl-2 expression in L-WOG group, M-WOG group and H-WOG group increased, while apoptosis rate, IL-1 β , IL-18, ROS, MDA, NLRP3 and Bax decreased ($P<0.05$). The OD_{490} , EdU positive cell rate, SOD, AMPK and Bcl-2 in WOG+Compound C group were lower than those in H-WOG group, and the apoptosis rate, IL-1 β , IL-18, ROS, MDA, NLRP3 and Bax expression were higher than those in H-WOG group ($P<0.05$). **Conclusion:** WOG can inhibit H/R-induced cardiomyocyte apoptosis, which may be relate to the AMPK/NLRP3 signaling pathway.

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前言

急性心肌梗死(AMI)是世界范围内常见的心血管疾病,是由心肌组织缺血引起,而心肌缺血是由于心肌代谢需求增加、冠状动脉循环向心肌组织供氧减少(缺氧)、营养物质减少导致^[1]。冠状动脉梗死再灌注可恢复血流和供氧,是AMI最有效的治疗方法。然而再灌注治疗也会导致进一步的细胞和组织损伤,这种情况称为缺氧/再氧合(H/R)损伤^[2]。H/R损伤的心肌细胞在AMI发生过程中发生炎症反应,进一步加重心肌损伤。研究表明,细胞凋亡、氧化应激、炎症反应在AMI发病机制中发挥重要作用^[3]。汉黄芩素(WOG)是黄芩根中提取的黄酮类化合物,具有抗炎、抗凋亡、抗氧化等作用,研究表明WOG可通过改善高脂饮食诱导的肥胖小鼠的心肌脂质代谢,减轻心肌细胞焦亡,进而减轻心脏损伤^[4]。单磷酸腺苷活化蛋白激酶(AMPK)在内皮细胞、骨骼肌、肝脏、大脑等多种细胞和组织中表达,在维持能量稳态、保护内皮细胞功能、调节细胞自噬、氧化应激等方面发挥重要作用,在当机体发生缺血或缺氧时,AMPK可激活促进血管生成^[5]。NOD样受体蛋白3(NLRP3)是一种胞质多蛋白复合物,当机体受到微生物感染、内源性危险信号和环境刺激时被激活,AMPK可以抑制NLRP3炎性小体的激活,在调节H/R诱导的心肌细胞焦亡、损伤中发挥重要作用^[6]。本研究探讨WOG对H/R诱导的心肌细胞凋亡的影响及其作用机制,现报道如下。

1 材料与方 法

1.1 材料及仪器来源

大鼠心肌细胞H9C2(货号:BJ-X1131,上海邦景实业有限公司);WOG[货号:53050ES10,翌圣生物科技(上海)股份有限公司];AMPK抑制剂Compound C(货号:8666430,上海研卉生物科技有限公司);噻唑蓝(MTT)细胞增殖检测试剂盒(货号:JC-A78381,上海机纯实业有限公司);5-乙炔基-2'-脱氧尿嘧啶核苷(EdU)法细胞增殖检测试剂盒(货号:KFS329-NCQ,北京百奥莱博科技有限公司);丙二醛(MDA)、活性氧类物质(ROS)、超氧化物歧化酶(SOD)、白介素(IL)-1 β 、IL-18酶联免疫吸附测定(ELISA)(货号:KS11466、KS13783、KS10400、KS12749、KS10711,上海科顺生物科技有限公司);总蛋白提取试剂盒、二喹啉甲酸法(BCA)蛋白定量试剂盒(货号:BB-3101、BB-3401,上海贝博生物科技有限公司);辣根过氧化物酶(HRP)、AMPK、NLRP3、Bcl-2、Bax、GAPDH抗体(货号:ab6802、ab32047、ab270449、ab241548、ab243140、ab128915,英国Abcam公司);无糖DMEM培养基、含糖DMEM培养基(货号:A1443001、10569010,美国赛默飞世尔公司);多功能酶联免疫分析仪(型号:Feyond A300,杭州奥盛仪器有限公司);流式细胞仪[型号:ZS-AE7S,中生(苏州)医疗科技有限公司]。

1.2 方 法

1.2.1 细胞培养与分组 H/R模型的构建^[7]:将H9C2细胞于无糖DMEM培养基中培养,并置于37℃下厌氧培养箱[95%氮气(N₂)和5%二氧化碳(CO₂)]中培养4h,将H9C2细胞至于含有4.5mm葡萄糖的DMEM中培养,并在37℃的正常培养箱[95%氧气(O₂)和5%CO₂]中培养24h,构建H/R模型。将H9C2细胞分为Control组(正常培养)、H/R组(H/R诱导)、L(低剂量)-WOG组、M(中剂量)-WOG组、H(高剂量)-WOG组(在H/R诱导的基础上分别加入40、80、120 μ mol/L的WOG^[8])、WOG+Compound C组(在H-WOG组基础上加入10 μ mol/L AMPK抑制剂Compound C^[9])。每组实验重复3次。

1.2.2 WOG对H9C2细胞增殖的影响 MTT法:将H9C2细胞以 1.5×10^3 个细胞/孔接种于96孔板培养12h后,每孔加入10 μ L 1.0 mg/mL的MTT溶液,在37℃、5%CO₂孵育4h,慢摇混合10min,采用多功能酶联免疫分析仪在490nm处测量吸光度。EdU染色:以 5×10^3 个/孔将H9C2细胞接种于96孔板中,加入50 μ L EdU孵育2h,固定染色后,于荧光显微镜下观察,计算EdU阳性细胞比例。

1.2.3 WOG对H9C2细胞凋亡的影响 将H9C2细胞以 5×10^4 个细胞/孔接种于12孔板,收集H9C2细胞重悬后,加入FITC-Annexin V/PI染色20min,在室温下避光孵育15min,用流式细胞仪进行分析。

1.2.4 ELISA法检测H9C2细胞血清氧化应激指标(MDA、ROS、SOD)和炎症因子(IL-1 β 、IL-18)水平 收集各组H9C2细胞,按照MDA、ROS、SOD、IL-1 β 、IL-18 ELISA试剂盒操作说明书检测H9C2细胞中MDA、ROS、SOD、IL-1 β 、IL-18的水平。

1.2.5 蛋白免疫印迹(WB)法检测H9C2细胞AMPK、NLRP3、Bcl-2、Bax蛋白表达 采用总蛋白提取试剂盒从H9C2细胞中提取总蛋白,采用BCA试剂盒检测蛋白浓度,用12%的十二烷基磺酸钠/聚丙烯酰胺凝胶电泳(SDS/PAGE)分离等量的蛋白质(30 μ g),然后转移到聚偏氟乙烯(PVDF)膜上,用5%脱脂牛奶封闭膜1h,用一抗AMPK(1:1000)、NLRP3(1:1000)、Bcl-2(1:1000)、Bax(1:500)、GAPDH(1:10000)在4℃下过夜,之后,用二抗(1:1000)孵育1h,使用增强型化学发光系统对蛋白带进行可视化,使用Image J软件进行分析。

1.3 统计学方法

数据采用SPSS 26.0软件进行分析。计量资料(AMPK、NLRP3蛋白表达等)以均值 \pm 标准差($\bar{x} \pm s$)表示,多组间比较采用单因素方差分析,两组间比较采用SNK-q检验。 $P < 0.05$ 表示有统计学意义。

2 结 果

2.1 WOG对H/R诱导的H9C2细胞增殖的影响

H/R组H9C2细胞的光密度值(OD₄₉₀)、EdU阳性细胞率低于Control组($P < 0.05$);与H/R组比较,L-WOG组、M-WOG组、H-WOG组OD₄₉₀、EdU阳性细胞率升高($P < 0.05$);

WOG+Compound C 组 OD₄₉₀、EdU 阳性细胞率低于 H-WOG 组 ($P<0.05$)。见图 1、表 1。

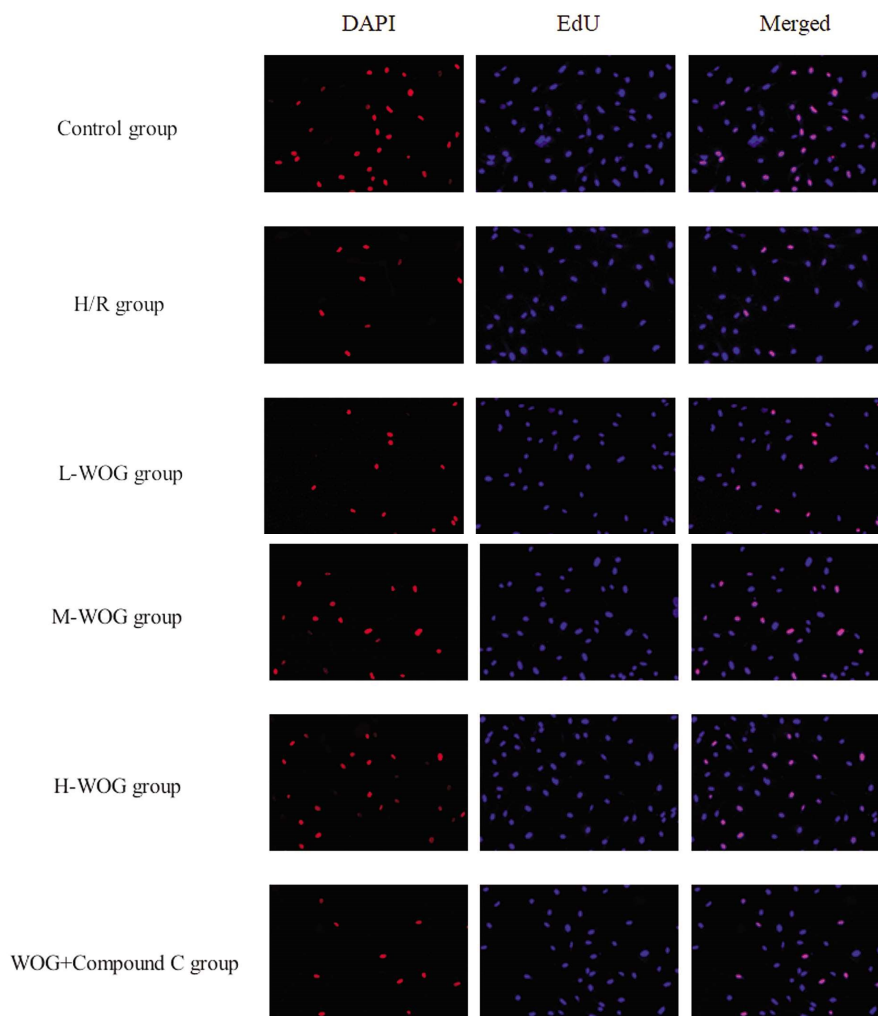


图 1 EdU 染色观察 H9C2 细胞增殖

Fig. 1 The proliferation of H9C2 cells was observed by EdU staining

表 1 WOG 对 H/R 诱导的 H9C2 细胞增殖的影响($\bar{x}\pm s, n=6$)

Table 1 Effect of WOG on H/R-induced H9C2 cell proliferation($\bar{x}\pm s, n=6$)

Groups	OD ₄₉₀	EdU positive cell rate(%)
Control group	1.46±0.15	45.31±4.60
H/R group	0.33±0.11 ^a	16.28±2.52 ^a
L-WOG group	0.64±0.12 ^b	25.34±3.07 ^b
M-WOG group	0.91±0.13 ^{bc}	33.19±3.89 ^{bc}
H-WOG group	1.25±0.14 ^{bcd}	42.96±4.44 ^{bcd}
WOG+Compound C group	0.58±0.11 ^c	23.01±2.73 ^c

Note: Compared with Control group, ^a $P<0.05$; Compared with H/R group, ^b $P<0.05$; Compared with L-WOG group, ^c $P<0.05$; Compared with M-WOG group, ^d $P<0.05$; Compared with H-WOG group, ^e $P<0.05$.

2.2 WOG 对 H/R 诱导的 H9C2 细胞凋亡的影响

H/R 组 H9C2 细胞的凋亡率高于 Control 组 ($P<0.05$); 与 H/R 组比较, L-WOG 组、M-WOG 组、H-WOG 组凋亡率降低 ($P<0.05$); WOG+Compound C 组凋亡率高于 H-WOG 组 ($P<0.05$)。见图 2、表 2。

2.3 WOG 对 H/R 诱导的 H9C2 细胞中 IL-1 β 、IL-18 表达的影响

H/R 组 H9C2 细胞中 IL-1 β 、IL-18 表达高于 Control 组

($P<0.05$); 与 H/R 组比较, L-WOG 组、M-WOG 组、H-WOG 组 IL-1 β 、IL-18 表达降低 ($P<0.05$); WOG+Compound C 组 IL-1 β 、IL-18 表达高于 H-WOG 组 ($P<0.05$)。见表 3。

2.4 WOG 对 H/R 诱导的 H9C2 细胞 MDA、ROS、SOD 表达的影响

H/R 组 H9C2 细胞 ROS、MDA 高于 Control 组, SOD 低于 Control 组 ($P<0.05$); 与 H/R 组比较, L-WOG 组、M-WOG 组、

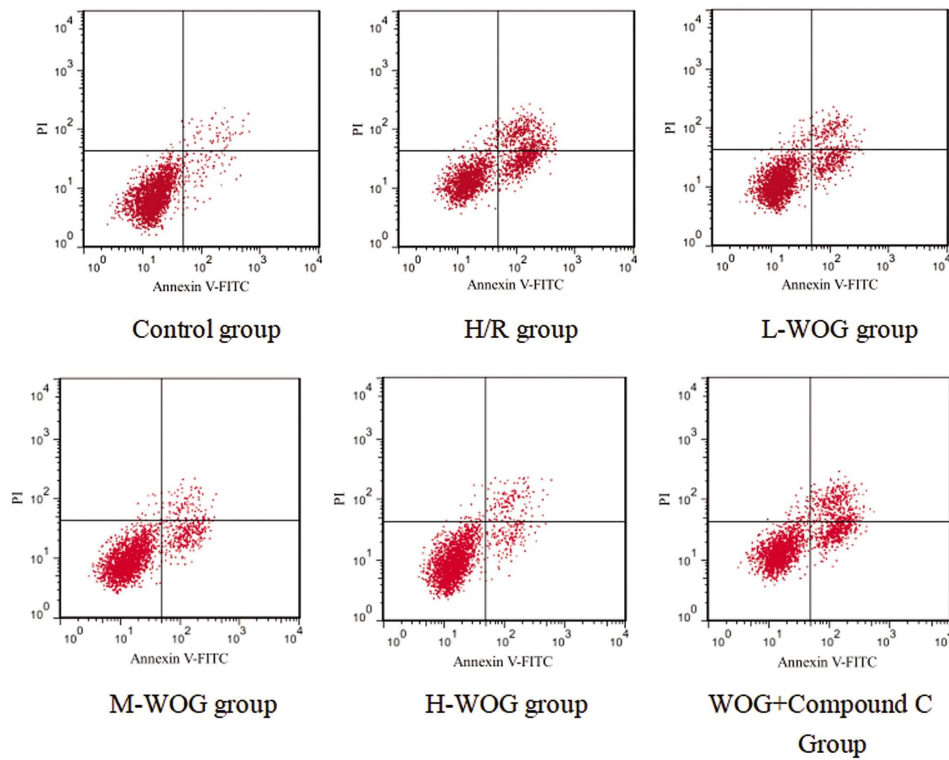


图 2 流式细胞仪检测 H9C2 细胞凋亡

Fig. 2 Apoptosis of H9C2 cells detected by flow cytometry

表 2 WOG 对 H/R 诱导的 H9C2 细胞凋亡的影响($\bar{x}\pm s, n=6$)

Table 2 Effects of WOG on H/R-induced apoptosis of H9C2 cells($\bar{x}\pm s, n=6$)

Groups	Apoptosis rate(%)
Control group	2.39±0.82
H/R group	47.90±4.79 ^a
L-WOG group	35.46±3.57 ^b
M-WOG group	22.17±2.78 ^{bc}
H-WOG group	10.35±2.46 ^{bcd}
WOG+Compound C group	40.52±3.82 ^c

Note: Compared with Control group, ^a $P<0.05$; Compared with H/R group, ^b $P<0.05$; Compared with L-WOG group, ^c $P<0.05$; Compared with M-WOG group, ^d $P<0.05$; Compared with H-WOG group, ^e $P<0.05$.

表 3 WOG 对 H/R 诱导的 H9C2 细胞中 IL-1 β 、IL-18 表达的影响($\bar{x}\pm s, n=6$)

Table 3 Effects of WOG on the expression of IL-1 β and IL-18 in H/R-induced H9C2 cells($\bar{x}\pm s, n=6$)

Groups	IL-1 β (pg/mL)	IL-18(pg/mL)
Control group	29.17±6.25	47.96±14.70
H/R group	117.36±12.09 ^a	190.17±19.85 ^a
L-WOG group	83.08±11.34 ^b	136.48±18.01 ^b
M-WOG group	54.51±9.82 ^{bc}	93.72±16.59 ^{bc}
H-WOG group	36.29±8.31 ^{bcd}	58.28±15.32 ^{bcd}
WOG+Compound C group	96.48±10.27 ^c	168.33±17.28 ^c

Note: Compared with Control group, ^a $P<0.05$; Compared with H/R group, ^b $P<0.05$; Compared with L-WOG group, ^c $P<0.05$; Compared with M-WOG group, ^d $P<0.05$; Compared with H-WOG group, ^e $P<0.05$.

H-WOG 组 ROS、MDA 降低, SOD 升高 ($P<0.05$); WOG+Compound C 组 ROS、MDA 高于 H-WOG 组, SOD 低于 H-WOG 组 ($P<0.05$)。见表 4。

2.5 WOG 对 H/R 诱导的 H9C2 细胞 AMPK、NLRP3、Bcl-2、Bax 表达的影响

H/R 组 NLRP3、Bax 高于 Control 组,AMPK、Bcl-2 低于 Control 组 (P 均 <0.05); 与 H/R 组比较,L-WOG 组、M-WOG

组、H-WOG 组 NLRP3、Bax 降低,AMPK、Bcl-2 升高 (P 均 <0.05);WOG+Compound C 组 NLRP3、Bax 高于 H-WOG 组,AMPK、Bcl-2 低于 H-WOG 组(P 均 <0.05)。见图 3、表 5。

表 4 WOG 对 H/R 诱导的 H9C2 细胞 MDA、ROS、SOD 表达的影响($\bar{x}\pm s, n=6$)

Table 4 Effects of WOG on the expression of MDA, ROS and SOD in H9C2 cells induced by H/R($\bar{x}\pm s, n=6$)

Groups	MDA(nmol/mL)	ROS(U/mL)	SOD(U/mL)
Control group	4.36±1.24	84.85±22.46	239.05±24.04
H/R group	73.25±8.07 ^a	269.71±27.38 ^a	64.28±19.47 ^a
L-WOG group	56.39±7.36 ^b	207.24±26.59 ^b	102.33±21.15 ^b
M-WOG group	25.18±5.47 ^{bc}	155.43±24.38 ^{bc}	145.54±22.32 ^{bc}
H-WOG group	11.24±2.59 ^{bcd}	99.82±23.17 ^{bcd}	189.76±23.13 ^{bcd}
WOG+Compound C group	60.28±6.21 ^c	244.74±25.32 ^c	88.09±20.59 ^c

Note: Compared with Control group, ^a $P<0.05$; Compared with H/R group, ^b $P<0.05$; Compared with L-WOG group, ^c $P<0.05$; Compared with M-WOG group, ^d $P<0.05$; Compared with H-WOG group, ^e $P<0.05$.

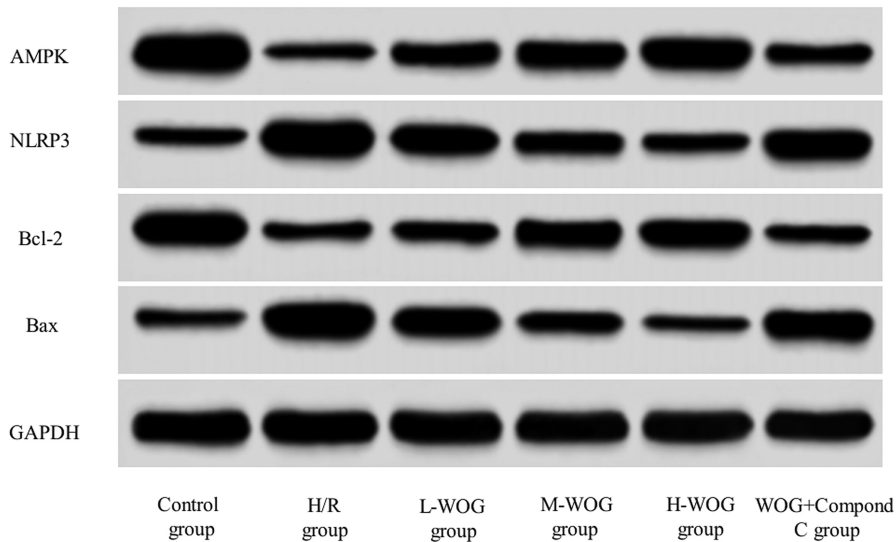


图 3 WB 检测 H9C2 细胞中 AMPK、NLRP3、Bcl-2、Bax 蛋白表达

Fig. 3 Expression of AMPK, NLRP3, Bcl-2 and Bax proteins in H9C2 cells was detected by WB

表 5 WOG 对 H/R 诱导的 H9C2 细胞 AMPK、NLRP3、Bcl-2、Bax 的影响($\bar{x}\pm s, n=6$)

Table 5 Effects of WOG on AMPK, NLRP3, Bcl-2 and Bax in H9C2 cells induced by H/R($\bar{x}\pm s, n=6$)

Groups	AMPK	NLRP3	Bcl-2	Bax
Control group	1.33±0.14	0.33±0.11	1.18±0.16	0.25±0.08
H/R group	0.29±0.09 ^a	1.29±0.16 ^a	0.34±0.11 ^a	1.21±0.13 ^a
L-WOG group	0.53±0.11 ^b	0.98±0.14 ^b	0.58±0.13 ^b	0.93±0.11 ^b
M-WOG group	0.74±0.12 ^{bc}	0.67±0.13 ^{bc}	0.81±0.14 ^{bc}	0.68±0.10 ^{bc}
H-WOG group	1.08±0.13 ^{bcd}	0.41±0.12 ^{bcd}	1.07±0.15 ^{bcd}	0.36±0.09 ^{bcd}
WOG+Compound C group	0.41±0.10 ^c	1.13±0.15 ^c	0.48±0.12 ^c	1.07±0.12 ^c

Note: Compared with Control group, ^a $P<0.05$; Compared with H/R group, ^b $P<0.05$; Compared with L-WOG group, ^c $P<0.05$; Compared with M-WOG group, ^d $P<0.05$; Compared with H-WOG group, ^e $P<0.05$.

3 讨论

AMI 已成为危害人类健康和生命的重大疾病之一,AMI

的发生风险受到多种因素如高血压、吸烟、冠状动脉疾病家族史以及艾滋病病毒、系统性红斑狼疮、阻塞性睡眠呼吸暂停等因素的影响^[10,11]。尽管近年对于 AMI 的药物治疗和介入技术研

究取得了一定进展,例如溶栓治疗、经皮冠状动脉介入治疗等干预措施可以迅速恢复缺血心肌的血液循环,限制心肌梗死的大小,还可避免心肌衰竭的发生。然而中断的血流恢复可能导致额外的心脏损伤和并发症,特别是心肌细胞的死亡,造成H/R损伤^[12]。据报道,ROS的过度积累与H/R损伤的发病机制有关,缺血期间ROS水平较低,血流再灌注时由于氧气回流导致ROS急剧上升,过量ROS可导致心肌细胞广泛的氧化损伤,促进炎症,加速心肌细胞凋亡^[13]。本研究发现,H/R诱导导致心肌细胞增殖能力下降,凋亡率升高,炎症因子和氧化应激指标水平升高,提示在H/R导致心肌细胞的氧化应激、炎症反应、心肌细胞凋亡增加,可能是AMI发生的重要原因。

WOG是中药黄芩活性成分之一,存在于黄芩的不同部位,具有抗炎、抗氧化以及抗肿瘤的作用^[14,15]。Shi等^[16]发现,WOG通过抑制人和大鼠心肌细胞的氧化应激,显著改善血管紧张素II诱导的心肌细胞肥大,并改善横主动脉收缩小鼠的心脏肥厚,可作为治疗心肌肥大的抗氧化剂。Xu等^[17]发现,WOG通过调节心肌细胞中的消皮素D蛋白减少顺铂诱导的袭击细胞焦亡,在体内可防止顺铂诱导的心功能障碍、心肌损伤、细胞焦亡,在减轻顺铂引起的心脏毒性方面具有较大的潜力。Wei等^[18]发现,WOG通过抑制线粒体细胞色素c的释放,减少天冬氨酸蛋白水解酶(caspase)激活引起的心肌细胞凋亡,从而保护大鼠心脏免受阿霉素损伤。Bei等^[19]发现,WOG可降低心肌梗死大小、心脏损伤因子、MDA、炎症因子的蛋白,对异丙肾上腺素诱导的心肌损伤具有强大的心脏保护活性。本研究发现,WOG可以抑制H/R诱导的氧化应激、炎症反应、心肌细胞凋亡,提示WOG可能通过抑制的氧化应激、炎症反应、心肌细胞凋亡进而抑制AMI的进展,提示WOG可作为治疗AMI的潜在药物。

AMPK是一种综合代谢传感器,在细胞水平上维持能量平衡,并协调组织间代谢信号传导,NLRP3炎症小体是先天免疫系统的关键组成部分,可介导caspase-1激活和促炎细胞因子IL-1 β 、IL-18的分泌^[20,21]。研究发现,NLRP3在AMI发生期间在心脏中积聚,并促进心肌损伤和细胞凋亡,而AMPK可抑制NLRP3的炎症反应^[6]。Zhang等^[22]发现,C1q肿瘤坏死因子相关蛋白9(CTRP9)可下调低密度脂蛋白活化巨噬细胞中NLRP3蛋白的表达,抑制AMPK则显著恢复NLRP3炎症小体的活性,CTRP9可通过AMPK/NLRP3通路发挥对动脉粥样硬化保护功能。Yao等^[23]发现,催产素通过AMPK/NLRP3信号通路提高了H/R后的细胞活力,并降低细胞凋亡、IL-18、IL-1 β 、NLRP3水平以及细胞焦亡相关蛋白的表达,进而减轻高血糖心肌I/R损伤。Wang等^[24]发现,龙胆苦苷通过激活AMPK抑制NLRP3炎症小体信号,减弱H/R诱导袭击的细胞死亡、ROS产生、乳酸脱氢酶和MDA释放以及抗氧化应激酶SOD活性,促炎细胞因子白细IL-6和肿瘤坏死因子- α 的转录和释放,在体内,龙胆苦苷能减轻H/R大鼠心脏结构异常、心肌细胞凋亡、心功能障碍,进而减轻H/R导致的心肌梗死和随后的心血管疾病。张晓蕾等^[25]发现,木犀草素通过激活AMPK/NLRP3信号通路,促进心肌细胞焦亡,对病毒心肌炎小鼠心肌发挥保护作用。本研究发现,H/R诱导心肌细胞中AMPK低表达,NLRP3高表

达,而WOG以浓度依赖的方式诱导AMPK高表达,抑制NLRP3表达,而AMPK抑制剂则可以逆转WOG对AMPK/NLRP3通路蛋白和心肌细胞增殖、凋亡的影响,提示WOG可能通过介导AMPK/NLRP3信号通路抑制H/R诱导的心肌细胞凋亡,进而抑制AMI的进展。

综上所述,WOG可以抑制H/R诱导的心肌细胞凋亡,其机制可能是介导AMPK/NLRP3信号通路实现的。本实验局限于AMPK/NLRP3信号通路相关因子且仅在细胞水平上进行验证,后期需完善实验方案继续研究。

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