康复学报
Rehabilitation Medicine

·临床研究·

冲击波联合核心稳定性训练对脑卒中非特异性腰背痛疗效观察

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摘要　目的　观察冲击波联合核心稳定性训练对脑卒中非特异性腰背痛(NLBP)的临床疗效。**方法**　选取2022年1月—2023年11月于苏州市相城人民医院就诊的70例脑卒中后NLBP患者为研究对象,采用随机数字表法将其分为对照组和试验组,每组35例。对照组接受常规治疗方案,根据患者病情选用红外线、脉冲调制中频电进行刺激,每项20 min/次;以及上下肢肌力、坐站位平衡、日常生活活动能力(ADL)和步行常规康复训练,40 min/次,5次/周,共治疗3周。试验组在对照组常规治疗的基础上接受冲击波训练,2次/周,共治疗3周;再进行核心稳定性训练,30 min/次,1次/d,5 d/周,共治疗3周。2组在治疗前、首次治疗后和治疗3周后应用视觉模拟疼痛量表(VAS)、Berg平衡量表(BBS)进行评估;使用超声波实时剪切波弹性成像技术在治疗前和治疗3周后评估腰部肌肉僵硬度的变化:使用足迹分析法测量患者的步行参数变化,比较2组的治疗效果。**结果**　与治疗前比较,首次治疗后和治疗3周后2组休息和步行状态下的VAS评分均降低,且试验组的VAS评分低于对照组($P<0.05$)。与对照组比较,试验组首次治疗后和治疗3周VAS评分明显下降($P<0.05$),试验组首次治疗后步行状态VAS评分下降($P<0.05$),治疗3周后步行状态VAS评分显著下降($P<0.001$)。治疗3周后,2组的腰方肌、竖脊肌、腰大肌硬度、BBS评分、步行参数(患侧平均步长、步幅及步速)均较本组治疗前改善,且试验组的改善幅度明显高于对照组($P<0.05$)。**结论**　冲击波联合核心稳定性训练能够减轻脑卒中后NLBP患者的疼痛症状,有效缓解腰背部肌肉的僵硬状态,并显著提升患者的平衡能力、改善步行表现。

关键词　脑卒中;非特异性腰背痛;冲击波;核心稳定性训练;步行能力

非特异性腰背痛(nonspecific low back pain,NLBP)是脑卒中后出现的慢性疼痛类型之一,临床特征包括腰背部酸胀疼痛、肌肉僵硬、运动受限及软弱无力,可能伴随下肢放射痛,这些症状严重影响了患者的生活质量、平衡和步行能力,甚至引发运动恐惧、废用和残疾[1]。脑卒中后NLBP的原因复杂而特殊[2],与平衡障碍、共同运动模式、偏瘫侧肢体活动不利和躯干肌肉力量减弱有关,迫使患者采取代偿性姿势进行日常活动,长期过度代偿导致肌肉劳损和肌肉疼痛。因此,脑卒中NLBP不仅仅需要解决疼痛问题,还需要关注躯干肌肉功能和腰椎稳定性的提升。当前临床治疗主要采用口服非甾

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体抗炎药以及脉冲调制中频电刺激、红外线等物理因子治疗来缓解疼痛。但常规治疗疗效缓慢，无法及时解决疼痛和反复发作，耽误偏瘫患者黄金期的恢复进度，对之后生活、工作造成严重影响。冲击波联合核心稳定性训练在肌骨系统中腰背痛应用疗效满意，所以本研究尝试将此治疗方案运用在脑卒中后NLBP，观察其与常规治疗的疗效对比。现将研究结果报告如下。

1 临床资料

1.1 病例选择标准

1.1.1 纳入标准 ① 符合《中国非特异性腰背痛临床诊疗指南》[3]有关下腰痛的诊断标准和《中国急性缺血性脑卒中诊治指南2018》[4]有关脑梗死的诊断标准或《中国脑出血诊治指南2019》[5]有关脑出血的诊断标准，并经MRI或CT确诊；② 遗留单侧肢体瘫痪；③ 可使用手杖或独立行走10 m以上；④ 腰背痛持续时间≥4周；⑤ 简易精神状态检查量表（mini-mental state examination，MMSE）评分≥24分；⑥ Brunnstrom分期Ⅲ～Ⅳ期。

1.1.2 排除标准 ① 腰部骨折后未稳定，治疗部位内有金属异物；② 同时存在严重的心血管疾病、糖尿病、强直性脊柱炎、类风湿性关节炎等；③ 之前使用止痛药、封闭治疗、小针刀等其他疗法治疗影响了本研究的结果；④ 有出血倾向或局部皮肤感染、破损。

1.2 一般资料

纳入2022年1月—2023年11月苏州市相城人民医院就诊的脑卒中后NLBP患者70例，采用随机数字表法分为对照组和试验组，每组35例。2组患者在性别、脑卒中病程、腰痛病程、脑卒中类型、脑卒中部位、年龄和体质量指数（body mass index，BMI）等一般资料比较，差异无统计学意义（$P>0.05$），具有可比性。见表1。本研究方案经苏州市相城人民医院医学伦理委员会批准通过（审批号：2023-KY-01），所有患者均顺利完成治疗，无脱落病例，每天积极主动完成医生制定的康复训练方案。

表1 2组一般资料比较

Table 1 Comparison of general data between two groups

组别	例数	性别(n,%)		病程/($\bar{x}\pm s$,月)		脑卒中类型(n,%)	
		男	女	脑卒中病程	NLBP病程	脑出血	脑梗死
对照组	35	16(45.71)	19(54.29)	6.11±2.72	2.45±0.73	13(37.14)	22(62.86)
试验组	35	13(37.14)	22(62.86)	5.84±2.61	2.50±0.48	11(31.43)	24(68.57)
χ^2/t值		0.530		0.424	-0.339	0.254	
P值		0.467		0.673	0.736	0.615	

组别	例数	脑卒中部位(n,%)			年龄/($\bar{x}\pm s$,岁)	BMI/($\bar{x}\pm s$,kg/m^2)
		丘脑	脑干	基底节		
对照组	35	10(28.57)	6(17.14)	19(54.29)	43.37±6.82	24.50±3.15
试验组	35	9(25.71)	9(25.71)	17(48.57)	42.33±6.65	24.25±3.30
χ^2/t值			0.764		0.646	0.324
P值			0.683		0.521	0.747

2 方 法

2.1 治疗方法

2.1.1 对照组 根据患者的病情一般选用红外线、脉冲调制中频电刺激。红外线：患者暴露治疗部位，灯头至于腰痛部位上方，灯距25～40 cm，患者感觉温热即可，20 min/次。中频电刺激：采用ZP-100cIVA型电脑中频治疗仪，将3 cm×3 cm的8个正方形电极依次排列置于腰部疼痛部位，20 min/次，腰背痛治疗处方，电流强度不超过患者的耐受量，以及上下肢肌力、坐站位平衡、日常生活活动能力（activities of daily living，ADL）和步行常规康复训练，40 min/次，每周5次，治疗3周。

2.1.2 试验组 在对照组的基础上增加冲击波和核心稳定性训练。

2.1.2.1 冲击波治疗 采用瑞士STORZ公司MP100放散式冲击波机，针对腰背部疼痛点进行冲击，避开重要神经和血管，骨关节处减轻力度。参数设置：电压6 kV，频率8～15 Hz，治疗压力1.5～3.0 bar，冲击次数为1 500～2 000次。每周治疗2次，连续进行3周。逐步增加治疗力度，从低到高，从低频到高频。年龄较大、体质较差或者比较敏感的患者要及时调整治疗强度和次数，避免皮肤破溃和局部淤肿等不良反应，提高患者治疗依从性。

2.1.2.2　核心稳定性训练　利用悬吊设备进行闭链测试,可制定针对薄弱的深层稳定肌的锻炼计划,通过逐步增加负荷来控制薄弱的肌肉回路。训练内容包括仰卧位、侧卧位、仰卧位、坐位和站立位,从两侧到偏瘫侧的重点强化和活动范围训练。训练将结合使用动态和静态闭链方法以及结合等长收缩,目的是加强多裂肌、臀中肌、臀大肌、内外斜肌、腹横肌、竖脊肌和其他肌群。训练中均匀呼吸。1次/d,30 min/次,5 d/周,训练3周。逐渐增加难度,循序渐进。训练过程中观察和监测患者的呼吸、心率、血压,并确保每个动作的正确性。

2.2　观察指标

分别在治疗前、首次治疗后和治疗3周后,由不知情分组的医师进行下列指标评估。

2.2.1　疼痛视觉模拟量表　在治疗前、首次治疗后及治疗3周后,评估在休息和步行状态下的腰痛程度。让患者根据自己的疼痛感觉在疼痛视觉模拟量表(visual analogue scale,VAS)评分上选择一个数字,其中0分代表无疼痛,10分代表最强烈的疼痛。

2.2.2　Berg平衡量表　Berg平衡量表(Berg balance scale,BBS)评分可用来评估患者的平衡能力。在治疗前以及治疗3周后,使用BBS评估患者的平衡能力,该量表由14个项目组成,涉及站立、坐下和自主站立。总分为56分,评分越高代表平衡能力越强,低于40分有跌倒危险[6]。

2.2.3　超声下肌肉的硬度　使用超声波实时剪切波弹性成像技术,通过计算剪切波的速度变化来定量测量组织硬度。采用频率5～14 MHz的线阵列探头,评估患者腰背段竖脊肌、腰方肌和腰大肌的肌肉硬度。硬度指标采用杨氏弹性模量(Young′s modulus),计算公式为$E=\sigma/\varepsilon$,σ表示正应力,ε表示正应变,E表示杨氏弹性模量,单位为kPa;系统自动算出目标区最大值、最小值及平均值,共测3次,计算平均E值。

2.2.4　步行参数　在治疗前和治疗3周后采用临床实践中广泛使用的足迹分析方法,对患者的步态参数进行比较。为此,要求患者在10 m长路径进行独立行走或使用手杖帮助行走。记录患侧的平均步长、步幅和步速3个参数,并进行3次测量和记录,然后计算其平均值。

2.3　统计学方法

采用SPSS 25.0统计学软件进行数据分析。计数资料采用χ^2检验;计量资料符合正态分布,用($\bar{x}\pm s$)表示,组间比较采用独立样本t检验,组内不同时间点的比较采用重复测量方差分析。$P<0.05$为差异有统计学意义。

3　结　果

3.1　2组治疗不同时间点休息和步行时的VAS评分比较

治疗前2组的休息和步行状态VAS评分比较,差异无统计学意义($P>0.05$);与治疗前比较,首次治疗后和治疗3周后,2组在休息和步行状态下的VAS评分均有所降低,试验组的VAS评分低于对照组($P<0.05$)。与对照组比较,试验组首次治疗和治疗3周后在休息状态下VAS评分明显下降($P<0.05$),试验组首次治疗后步行状态VAS评分下降($P<0.05$),治疗3周后步行状态VAS评分显著下降($P<0.001$)。和治疗结束3个月后回访,发现试验组复发3例,对照组复发8例,试验组复发率低于对照组,但差异无统计学意义($P>0.05$)。见表2。

表2　2组治疗前后VAS评分和复发例数比较($\bar{x}\pm s$)

Table 2　Comparison of VAS scores and number of relapse cases between two groups before and after treatment ($\bar{x}\pm s$)

组别	例数	休息状态VAS/[($\bar{x}\pm s$),分]			步行状态VAS/[($\bar{x}\pm s$),分]			复发例数
		治疗前	首次治疗后	治疗3周	治疗前	首次治疗后	治疗3周	
对照组	35	5.2±1.2	4.8±0.5	3.5±0.5	6.3±1.7	5.8±1.1	5.1±0.6	8
试验组	35	5.4±1.3	4.5±0.5	3.2±0.4	6.5±1.8	5.2±1.2	4.5±0.7	3
χ^2/t值		0.669	−2.510	−2.772	0.478	−2.181	−3.850	2.696
P值		0.506	0.015	0.007	0.634	0.033	<0.001	0.101

3.2　2组治疗前后超声弹性成像技术下腰部肌肉硬度比较

治疗前2组腰方肌、竖脊肌、腰大肌硬度比较差异无统计学意义($P>0.05$)。治疗3周后,试验组腰部肌肉僵硬程度改善较对照组更明显($P<0.05$)。见表3。

3.3　2组治疗前后步态参数和BBS评分比较

治疗前2组平均步长、步宽、步速比较,差异无统计学意义($P>0.05$)。治疗3周后,试验组的步长、步速均高于对照组($P<0.05$);步宽低于对照组($P<0.05$)。治疗前2组BBS评分比较,差异无统计学意义($P>0.05$)。治疗3周后,试验组的BBS评

分优于对照组(P<0.05)。见表4。

表3 2组治疗前肌肉硬度比较($\bar{x}\pm s$) kPa

Table 3 Comparison of muscle hardness stiffness between two groups before and after treatment ($\bar{x}\pm s$) kPa

组别	例数	腰方肌		竖脊肌		腰大肌	
		治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
对照组	35	28.31±2.52	17.52±2.18	34.34±2.80	19.50±2.61	30.72±3.55	18.47±2.90
试验组	35	27.90±2.44	12.23±1.56	34.95±3.76	15.18±2.47	31.28±3.14	14.34±1.81
t值		-0.692	-11.675	0.770	-7.112	0.699	-9.311
P值		0.492	<0.001	0.444	<0.001	0.487	<0.001

表4 2组治疗前后步长、步宽、步速和BBS评分比较($\bar{x}\pm s$)

Table 4 Comparison of step length, step width, step speed and BBS scores between two groups before and after treatment ($\bar{x}\pm s$)

组别	例数	步长/cm		步宽/cm		步速/(cm/s)		BBS/分	
		治疗前	治疗后	治疗前	治疗后	治疗前	治疗后	治疗前	治疗3周
对照组	35	31.62±3.34	36.50±2.62	10.54±2.12	8.17±1.33	30.77±3.20	38.21±2.43	16.42±2.28	34.12±2.17
试验组	35	31.50±3.65	41.28±2.54	10.65±2.66	7.28±1.54	31.04±3.62	41.55±2.87	16.59±2.16	36.14±2.74
t值		-0.143	7.750	0.191	-2.588	0.331	5.254	0.320	3.419
P值		0.886	<0.001	0.849	0.012	0.742	<0.001	0.750	0.001

4 讨论

4.1 冲击波联合核心稳定性训练对脑卒中后NLBP疼痛的影响

本研究证实,2组均能减轻脑卒中后NLBP患者腰部疼痛,而试验组的训练效果更具优势。周明等[7]发现使用冲击波治疗可改善腰痛患者的疼痛评分和功能评估。樊乐等[8]研究显示,NLBP患者接受了冲击波治疗后,VAS评分、Oswestry下腰痛功能障碍指数(Oswestry low back pain dysfunction index,ODI)均低于治疗前和对照组。张欣[9]研究表明,桥式运动等核心训练可促进内源性β-内啡肽的产生,β-内啡肽与阿片受体结合后,具有镇痛、躯体保护、抗炎和抗过敏等多重作用[10],同时能够降低血清皮质醇水平,从而防止长期压力引起的背痛对身体的负面影响。这与本研究结果一致,试验组在休息和步行状态下VAS评分均低于治疗前和对照组,进一步证明了冲击波联合核心稳定性训练在减轻NLBP患者疼痛方面的有效性。本研究还发现,首次治疗后以及治疗3周后的数据表明,试验组在减轻疼痛方面的效果优于对照组。这说明虽然2种方法都能减轻疼痛,但试验组的即时止痛效果和短期效果更具优势。这与冲击波的机械应力效应和空化效应有关,高能量的冲击波对神经感受器产生强刺激作用,进而达到镇痛的效果。同时脑卒中后NLBP患者中枢神经系统对躯干肌肉的神经支配受损,导致躯干肌肉萎缩和肌肉横截面积缩小的现象,进一步加剧疼痛。国内外相关研究也都表明NLBP患者存在腰部肌力和腰椎稳定性降低问题[11]。这种腰椎稳定肌肉的萎缩和功能障碍,以及慢性疼痛导致的中枢反射抑制和神经系统的控制障碍,共同导致了"萎缩-疼痛-活动受限"的恶性循环。而核心稳定性训练不仅能够增强脊柱的稳定性,还能通过提高β-内啡肽和皮质醇的水平,抑制疼痛信息的传递,从而有效缓解疼痛。此外,本研究结果显示,在随访期间,对照组复发8例,而试验组复发3例,试验组复发率低于对照组,但差异无统计学意义(P>0.05)。这表明常规的物理治疗虽然能够缓解疼痛、改善腰部功能,但其疗效并不持久,未能从根本上解决腰痛的原因,不利于腰痛的复发和预防。而脑卒中后NLBP不只表现为即刻疼痛,还与中枢神经系统控制减弱以及运动策略调整有关。核心稳定性训练可以增强偏瘫侧躯干肌肉力量,提高腰椎稳定性,减少代偿动作,达到治疗NLBP的长期效果。

4.2 冲击波联合核心稳定性训练对脑卒中后NLBP腰部肌肉硬度的影响

治疗3周后,利用肌骨超声实时剪切波弹性成像技术观察到,相较于对照组,试验组的E值降低,腰方肌、竖脊肌和腰大肌的硬度下降幅度更大,表明冲击波治疗联合核心稳定性训练可以有效缓解局部僵硬状态,使疼痛紧张的肌肉在治疗后硬度降低。CHEN等[12]运用磁共振弹性成像技术,发现筋膜痛患者的紧张带硬度比周围正常肌肉组织高出

约50%,冲击波在治疗各种腱病时,不仅能抑制疼痛,还能通过刺激新生血管形成,进而影响微循环,达到长期的临床疗效。陈波等[13]的研究也显示,冲击波治疗后,患者紧张带的硬度与周围肌肉组织相比降低,这与本研究的结果相吻合。冲击波穿透组织时,组织中的小气泡迅速膨胀,释放更多热量至密闭空间,进而增加血管内皮生长因子(vascular endothelianl growth factor,VEGF)、内皮型一氧化氮合酶(endothelial nitric oxide synthase,eNOS)等因子的表达,从而改善局部血液循环。此外,冲击波还能通过改变突触前后膜上的受体或递质分解酶,调节疼痛神经递质的释放和再摄取,进而调节神经信号的传递,降低机体的疼痛敏感性。FRIZZIERO等[14]认为增强慢性腰痛患者躯干的稳定性有助于减轻疼痛和功能限制。核心稳定性训练能够锻炼躯干、骨盆和腹部的所有肌肉,有效激活腰背部深层小肌肉,提高未使用或萎缩的躯干肌肉的激活率,加快肌肉募集。核心稳定性训练还增强腰背部力量,提高全身血液循环,纠正左右腰背部肌肉的不平衡和偏瘫患者不良代偿姿势,有效缓解腰背部僵硬状态,改善腰部的柔韧性和灵活性。

4.3 冲击波联合核心稳定性训练对脑卒中后NLBP步行参数和平衡的影响

NLBP相较于偏瘫性肩痛和肌肉痉挛痛,其发生更为隐匿。由于躯干肌群受到双侧神经元的支配,脑卒中后早期并不会出现明显的躯干肌群瘫痪,这导致多数患者无法及时获得诊断与有效治疗。在恢复期,为了代偿肢体的功能障碍,患者常出现前倾、侧身、重心偏移等动作,进而引发躯干肌肉不平衡和疼痛,疼痛又进一步加剧平衡控制能力的下降。脑卒中后NLBP患者为减轻地面反作用力对腰椎骨盆区域造成的疼痛冲击,常采取适应性步行策略[15],表现为步行速度较正常人慢,步长较短,步宽较大。KIM等[16]的报告指出躯干肌肉力量的衰弱与慢性中风患者的功能表现密切相关,核心力量锻炼有助于改善中风患者的步态和平衡[17],HODGES和RICHARDSON认为[18],腰椎稳定性在诱导下肢运动中发挥重要作用,提升躯干调节能力有助于提高动态平衡、步态速度以及中风患者步态期间的躯干对称性。MADADI-SHAD等[19]通过设计的纠正性训练使NLBP患者在干预后疼痛减轻并表现出更快的步速,这与本研究结果一致。治疗3周后,相较于对照组,试验组的平衡功能及平均步长、步宽及步速等方面均表现出更大的改善幅度。冲击波的快速缓解疼痛作用有助于减轻患者的疼痛恐惧心理,使其能更好地参与康复训练。核心稳定性训练则能有效提升中枢神经系统对运动的控制能力和本体感觉输入能力,进而增强对偏瘫侧的控制能力,改善平衡及下肢运动控制能力,优化步态参数,减少躯干代偿性使用,降低躯干肌肉疲劳。

综上所述,冲击波联合核心稳定性训练治疗能够减轻脑卒中后NLBP患者的疼痛症状,有效缓解腰背部肌肉的僵硬状态,并显著提升患者的平衡能力,改善其步行表现,其临床效果优于传统的物理治疗方法。此外,本研究在治疗前对患者的凝血功能、心电图以及血压等进行了全面检查,治疗过程中密切关注患者的主观感受,确保操作远离神经血管,避免直接接触骨性组织,从而有效预防不良事件的发生,实现了治疗的精准定位,减少了盲打操作的发生率。患者对治疗流程满意度高,治疗过程中未出现肿胀、疼痛加剧或血肿等并发症。但本研究患者样本量有限,观察的下肢步态参数指标相对简单,未通过三维步态分析整个步行周期的变化,对于足底压力、脊柱骨盆的活动范围没有监测和分析。在后续的研究中将进一步扩大样本,开展多中心深入的研究。

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Efficacy of Shock Wave Therapy Combined with Core Stability Training on Non-Specific Low Back Pain after Stroke

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ABSTRACT **Objective** To investigate the clinical efficacy of shock wave therapy combined with core stability training on non-specific low back pain (NLBP) after stroke. **Methods** A total of 70 patients with post-stroke NLBP who visited Suzhou Xiangcheng People's Hospital from January 2022 to November 2023 were selected as the subjects of the study. They were randomly assigned to control group and experimental group, wich 35 cases in each group. The control group received conventional treatment, which included infrared and pulse-modulated medium-frequency electrical stimulation, 20 minutes per session; as well as regular rehabilitation training for muscle strength of upper and lower limbs, sitting and standing balance, activities of daily living (ADL), and walking, 40 minutes per session, 5 times per week, for a total of 3 weeks. The experimental group, in addition to the conventional treatment of the control group, received shock wave therapy, 2 times per week for a total of 3 weeks; followed by core stability training, 30 minutes per session, once a day, 5 days per week, for a total of 3 weeks. Visual analogue scale (VAS) for pain, Berg balance scale (BBS) were assessed before treatment, after the first treatment, and after 3 weeks of treatment in both groups, and changes in the stiffness of waist muscles (E-mean) assessed by ultrasound real-time shear wave elastography were compared before treatment and after 3 weeks of treatment in both groups. Additionally, gait parameters were measured using footprint gait analysis to compare the

therapeutic effects of the two groups. **Results** Compared with those before treatment, VAS scores of both groups decreased at rest and during walking after the first treatment and after 3 weeks of treatment, with the experimental group showing significantly lower VAS scores than the control group (P<0.05). Compared with the control group, the VAS scores of the experimental group decreased significantly after the first treatment and 3 weeks of treatment (P<0.05), and the VAS scores of the experimental group decreased significantly after the first treatment (P<0.05) and after 3 weeks of treatment (P<0.001). After 3 weeks of treatment, the hardness of the quadratus lumborum, erector spinae, and psoas major muscles, BBS scores, and gait parameters (average step length, step width, and walking speed on the affected side) of both groups improved compared to those before treatment, with the experimental group showing a significantly greater improvement than the control group (P<0.05). **Conclusion** The combination of shock wave therapy and core stability training can effectively alleviate pain symptoms in patients with post-stroke NLBP, significantly reduce the stiffness of the lumbar and back muscles, and markedly improve balance ability and walking performance.
KEY WORDS stroke; non-specific low back pain; radial shock wave; core stability training; gait ability
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Mechanism of Qingjie Fuzheng Granules on Alleviating 5-FU Chemotherapy-Induced Intestinal Mucositis in Mouse Model of Colorectal Cancer By Regulating Cathepsin B/NLRP3 Pathway

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ABSTRACT **Objective** To explore the therapeutic effect and underlying mechanism of Qingjie Fuzheng Granules (QFG) on intestinal mucositis caused by 5-fluorouracil (5-FU) chemotherapy in mice with colorectal carcinoma based on the Cathepsin B/NLRP3 pathway. **Methods** A total of twenty-four male BALB/c mice were selected for subcutaneous inoculation of CT26 cells in the axilla of the right forelimb to construct a subcutaneous graft mouse model of colorectal carcinoma. When the tumor volume grew to 100-300 mm^3, the mice were randomly divided into control group, 5-FU group, and 5-FU+Qingjie Fuzheng Granule group (5-FU+QFG group), with 8 mice in each group. The control group was given saline gavage and intraperitoneal injection, and mice in the other groups received intraperitoneal injection of 5-FU (50 $mg/kg·d^{-1}$), once daily for 5 days; the 5-FU+QFG group was given Qingjie Fuzheng Granules (1.0 $g/kg·d^{-1}$) by gavage during chemotherapy, once daily for 7 days. Mice were observed daily for diarrhea, and their body mass and tumor volume were recorded. After the last administration on the 7th day, the mice were fasted for 12 hours, and then sampled and tested.The histopathological changes in the jejunum were observed by hematoxylin-eosin staining (HE); the expression levels of diamine oxidase (DAO), D-lactic acid (D-LA), endotoxin (ET), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6) were measured by enzyme-linked immunosorbent assay (ELISA); the positive expression of Cathepsin B in the jejunal tissue was detected by immunohistochemistry; the relative expression level of tight junction protein ZO-1 and Occludin mRNA in jejunal tissue were determined by real-time quantitative polymerase chain reaction (RT-qPCR), and the relative expression level of ZO-1, Occludin, Cathepsin B, NLRP3, ASC, and cleaved Caspase-1 protein in the jejunal tissue were determined by the Western blot method. **Results** (1) General condition of mice: During the experimental period, QFG significantly reduced the diarrhea symptoms caused by 5-FU chemotherapy (P<0.05), had no significant improvement on body weight loss caused by 5-FU chemotherapy (P>0.05), and had no significant synergistic effect on tumor growth inhibition by 5-FU (P>0.05). (2) Histopathological changes of jejunum: QFG significantly improved the symptoms of intestinal mucosal injury such as shortening of intestinal mucosal villi, deepening of crypts and inflammatory cell infiltration caused by 5-FU chemotherapy. (3) Serum DAO, D-LA, ET, and TNF-α, IL-1β, IL-6 content: Compared with the 5-FU group, QFG significantly reduced the serum content of DAO, D-LA, E-T, and pro-inflammatory cytokines TNF-α, IL-1β, IL-6 in the serum of mice with colon cancer (P<0.05). (4) Protein expression levels of Cathepsin B, NLRP3, ASC, and cleaved Caspase-1 in jejunal tissue: Compared with the 5-FU group, QFG significantly reduced the relative protein expression of Cathepsin B (P<0.05) and reduced the relative protein expression of NLRP3, ASC and cleaved Caspase-1 in jejunal tissue (P<0.05). (5) ZO-1 and Occludin mRNA transcription levels and protein expression levels in jejunal tissue: Compared with the 5-FU group, QFG significantly increased the mRNA and relative protein expressions of tight junction proteins ZO-1, Occludin in the 5-FU+QFG group (P<0.05). **Conclusion** By regulating Cathepsin B/NLRP3 signaling pathway, reducing proinflammatory cytokine release, inhibiting intestinal mucosal inflammatory responses, and repairing intestinal mucosal barrier damage, Qingjie Fuzheng Granules can alleviate chemotherapeutic intestinal mucositis caused by 5-FU.
KEY WORDS colorectal cancer; Cathepsin B/NLRP3; intestinal mucositis; 5-fluorouracil; Qingjie Fuzheng Granules
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