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腰椎间盘突出症患者血清SDF-1、MMP3、IL-1β水平与椎间盘退变分级的相关性分析

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摘要 目的：探讨血清基质细胞衍生因子(SDF-1)、基质金属蛋白酶-3(MMP3)、白细胞介素-1β(IL-1β)与腰椎间盘突出症(LDH)患者椎间盘退变分级的相关性。方法：选取2020年7月至2022年7月武汉市第三医院收治的LDH患者150例作为观察组，另选同期90例体检为正常椎间盘组织作为健康对照组；对比两组血清SDF-1、MMP3、IL-1β表达水平；参照Pfirrmann分级标准将观察组患者分为椎间盘退变Ⅲ级、Ⅳ级、Ⅴ级，对比L4/5、L5/S1节段椎间盘退变不同级别的血清SDF-1、MMP3、IL-1β表达水平，并采用Spearman相关性分析方法分析血清SDF-1、MMP3、IL-1β表达水平与L4/5、L5/S1节段椎间盘退变分级的相关性。结果：观察组血清SDF-1、MMP3、IL-1β水平均高于对照组($P<0.05$)。L4/5、L5/S1节段不同腰椎间盘分级椎间盘突出症患者各亚组血清中SDF-1、MMP3、IL-1β水平随着病变程度增加而升高(分别为$F=68.867$、47.578、212.079和$F=221.461$、346.920、514.849；$P<0.05$)。Spearman相关性分析结果显示：血清SDF-1、MMP3、IL-1β水平与L4/5、L5/S1节段腰椎间盘分级均呈正相关(分别为$r=0.759$、0.801、0.785和$r=0.748$、0.823、0.816；$P<0.05$)。结论：血清SDF-1、MMP3、IL-1β表达水平与腰椎间盘退变程度呈正相关，随着病情加重，其表达水平升高，提示血清血清SDF-1、MMP3、IL-1β水平与腰椎间盘退变的发生发展密切相关。

关键词 基质细胞衍生因子；基质金属蛋白酶-3；白细胞介素-1β；腰椎间盘突出症；椎间盘退变分级；炎症因子
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Correlation analysis between serum SDF-1, MMP 3, IL-1β and grade of intervertebral disc degeneration in patients with lumbar disc herniation

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Abstract

Objective: To investigate the correlation between serum stromal cell-derived factor 1 (SDF-1), matrix metalloproteinase-3 (MMP-3), interleukin-1β (IL-1β), and the grade of intervertebral disc degeneration in patients with lumbar disc herniation(LDH). **Methods:** A total of 150 LDH patients admitted to our hospital from July 2020 to July 2022 were selected as the observation group, and another 90 healthy individuals with normal intervertebral disc tissue were selected as the healthy control group. The expression levels of serum SDF-1, MMP3, and IL-1β were compared between the two groups. The observation group was classified into Grade Ⅲ, Grade Ⅳ, and Grade Ⅴ of disc degener-

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ation according to the Pfirrmann classification standard. The expression levels of serum SDF-1, MMP3, and IL-1β were compared among the different subgroups of disc herniation patients, respectively, at L4/5 and L5/S1 segments. Spearman's correlation analysis was performed to assess the relationship between the expression levels of serum SDF-1, MMP3, and IL-1β and the degeneration grade of intervertebral discs at L4/5 and L5/S1 segments. **Results:** The levels of serum SDF-1, MMP3, and IL-1β in the observation group were higher than those in the control group ($P<0.05$). Serum SDF-1, MMP3, IL-1β in different subgroups of patients with lumbar disc herniation at L4/5 and L5/S1 segments increased with the degree of lesion ($F=68.867, 47.578, 212.079$; $F=221.461, 346.920, 514.849$; $P<0.05$). Spearman correlation analysis showed that the level of sserum SDF-1, MMP3, and IL-1β was positively correlated with L4/5 and L5/S1 lumbar disc classification ($r=0.759, 0.801, 0.785$; $r=0.748, 0.823, 0.816$; $P<0.05$). **Conclusion:** The expression level of serum SDF-1, MMP3, and IL-1β was positively correlated with the degree of degeneration of the lumbar intervertebral disc. As the severity of the disease increases, their expression levels rise, suggesting a close association between serum levels of SDF-1, MMP3, and IL-1β and the development of lumbar disc degeneration.

Key Words Stromal Cell Derived Factor 1; Matrix Metalloproteinase-3; Interleukin-1β; Lumbar Disc Herniation; Classification of Intervertebral Disc Degeneration; Inflammatory Factor

腰椎间盘突出(lumbar disc herniation,LDH)患者腰间盘各部分特别是髓核出现不同程度的退行性改变,使得相邻脊神经根遭受刺激或压迫[1-2]。临床主要表现为腰部疼痛、单侧下肢或双下肢麻木、疼痛等,多发于腰4～5(L4/5)、腰5～骶1(L5/S1)[3]。椎间盘退行性病变受多种因素影响,如生物结构力学、生物化学、分子学、血液循环等[4-5]。基质细胞衍生因子(stromal-derived factor,SDF-1)是一类对免疫细胞有趋化作用的小分子蛋白质,已有学者[6]研究发现SDF-1可参与椎间盘生物学功能的重建和恢复。基质金属蛋白酶-3(matrix metalloproteinase-3,MMP3)是由成纤维细胞、毛细血管内皮细胞和其他结缔组织细胞产生,与椎间盘的退变密切相关[7]。白细胞介素-1β(interleukin-1β,IL-1β)已被证实是一种强烈的致痛物质,可诱导发生痛觉,有研究显示退行性病变椎间盘髓核中IL-1β水平升高,IL-1β可能参与促进腰椎间盘退行性病变的发病机制[8]。然而,血清中上述因子的表达水平与椎间盘退变分级的相关性尚无定论。基于此,本研究通过对比不同椎间盘退变分级患者血清SDF-1、MMP3、IL-1β水平,分析其相关性,以期为临床判断LDH分级情况提供参考。

1 资料与方法

1.1 一般资料 观察组病例来自武汉市第三医院2020年7月至2022年7月收治的150例腰椎间盘退变性疾病患者。入组标准:(1)符合文献[9]中关于LDH的诊断标准;(2)腰椎侧位X光片显示:上椎间位移3 mm以上,无椎间角度变化;(3)表现为腰腿疼痛、肢体麻木或不适、肌力减退等。排除标准:(1)接受过腰椎手术治疗,且腰椎存在退变性不稳者;(2)严重风湿病、糖尿病、骨质疏松、恶性肿瘤者;(3)脊柱感染、脊柱骨折、先天性腰椎滑脱者;(4)合并各关节骨关节炎者。其中:男58例,女92例;年龄40～75(60.59±7.16)岁;L4/5节段腰椎间盘退变分级:Ⅲ级45例、Ⅳ级80例、Ⅴ级25例;L5/S1节段腰椎间盘退变分级:Ⅲ级54例、Ⅳ级63例、Ⅴ级33例。另选同期90例体检为正常椎间盘组织作为健康对照组,其中男38例,女52例,年龄38～72(59.86±7.52)岁。两组一般资料比较,差异均无统计学意义($P>0.05$)。

1.2 观察指标

1.2.1 腰椎间盘退变MRI分级 采用3.0 T MRI系统(飞利浦GE)对患者进行腰椎间盘检测,检查结果由两名影像科医师独立分析,并对L4/5和L5/S1节段图像分级。参照Pfirrmann的MRI分级标准分级,其中:Ⅰ级多发生在儿童人群,本研究病例为中老年患者,因此,定义Ⅱ级为正常椎间盘,Ⅲ～Ⅴ级为退变椎间盘。

1.2.2 血清学指标水平 采集所有患者入院后和对照组体检时空腹静脉血,常规离心分离后取上清

液，采用酶联免疫吸附法检测 SDF-1、MMP3 及 IL-1β 水平。严格按照试剂盒（北京中杉金桥生物技术有限公司）说明书进行操作。

1.3　统计学方法　SPSS 20.0 分析本研究数据，计量资料用均数±标准差（$\bar{x}\pm s$）表示，行 t 检验；计数资料用“例（%）”表示，行 χ^2 检验；采用 Spearman 相关性分析法评估血清 SDF-1、MMP3、IL-1β 与腰椎间盘突出症患者椎间盘退变分级的相关性分析；以 $P<0.05$ 为差异有统计学意义。

2　结果

2.1　两组血清 SDF-1、MMP3、IL-1β 水平　观察组血清 SDF-1、MMP3、IL-1β 水平均高于对照组（$P<0.05$）。见表 1。

表 1　两组血清 SDF-1、MMP3、IL-1β 水平对比（$\bar{x}\pm s$）

组别	例数	SDF-1/μg•L^{-1}	MMP3/μg•L^{-1}	IL-1β/ng•L^{-1}
观察组	150	24.43±2.82	35.65±4.08	11.86±1.70
对照组	90	10.01±1.56	11.92±1.53	3.29±0.56
t	—	44.568	52.952	46.307
P	—	<0.001	<0.001	<0.001

2.2　L4/5 节段不同腰椎间盘分级患者血清 SDF-1、MMP3、IL-1β 水平对比　L4/5 节段不同腰椎间盘分级患者各亚组血清中 SDF-1、MMP3、IL-1β 水平随着病变程度增加而升高（$F=68.867$、47.578、212.079，$P<0.05$）。见表 2。

表 2　L4/5 节段不同腰椎间盘分级患者血清 SDF-1、MMP3、IL-1β 水平对比（$\bar{x}\pm s$）

分级	例数	SDF-1/μg•L^{-1}	MMP3/μg•L^{-1}	IL-1β/ng•L^{-1}
Ⅲ级	45	20.64±3.06	30.64±4.09	8.64±1.68
Ⅳ级	80	24.62±3.38^{a}	36.62±4.57^{a}	11.62±1.96^{a}
Ⅴ级	25	30.64±4.12^{ab}	41.56±5.86^{ab}	18.60±2.32^{ab}
F	—	68.867	47.578	212.079
P	—	<0.001	<0.001	<0.001

与Ⅲ级比，$^{a}P<0.05$；与Ⅳ级比，$^{b}P<0.05$

2.3　L5/S1 节段不同腰椎间盘分级患者血清 SDF-1、MMP3、IL-1β 水平对比　L5/S1 节段不同腰椎间盘分级患者各亚组血清中 SDF-1、MMP3、IL-1β 水平随着病变程度增加而升高（$F=221.461$、346.920、514.849，$P<0.05$）。见表 3。

表 3　L5/S1 节段不同腰椎间盘分级患者血清 SDF-1、MMP3、IL-1β 水平对比（$\bar{x}\pm s$）

分级	例数	SDF-1/μg•L^{-1}	MMP3/μg•L^{-1}	IL-1β/ng•L^{-1}
Ⅲ级	54	21.03±2.76	31.30±4.21	9.06±1.28
Ⅳ级	63	25.76±3.21^{a}	35.15±4.25^{a}	12.18±1.56^{a}
Ⅴ级	33	36.24±4.12^{ab}	57.71±6.28^{ab}	20.89±2.38^{ab}
F	—	221.461	346.920	514.849
P	—	<0.001	<0.001	<0.001

与Ⅲ级比，$^{a}P<0.05$；与Ⅳ级比，$^{b}P<0.05$

2.4　血清 SDF-1、MMP3、IL-1β 水平与 L4/5、L5/S1 节段腰椎间盘分级的相关性　Spearman 相关性分析结果显示：血清 SDF-1、MMP3、IL-1β 水平与 L4/5、L5/S1 节段腰椎间盘分级均呈正相关（分别为 $r=0.759$、0.801、0.785 和 $r=0.748$、0.823、0.816，$P<0.05$）。见表 4。

表 4　血清 SDF-1、MMP3、IL-1β 水平与 L4/5、L5/S1 节段腰椎间盘分级的相关性

变量	L4/5 节段腰椎间盘分级		L5/S1 节段腰椎间盘分级	
	r	P	r	P
SDF-1/μg•L^{-1}	0.759	<0.001	0.748	<0.001
MMP3/μg•L^{-1}	0.801	<0.001	0.823	<0.001
IL-1β/ng•L^{-1}	0.785	<0.001	0.816	<0.001

3　讨论

腰椎间盘退变与多种因素有关，如炎症因子、氧化应激、生物力学等[10]。研究[11]发现，SDF-1 在成人的毛细血管新生中发挥重要作用，缺氧状态下，SDF-1 大量增加，可增加血管内皮生长因子的表达水平；SDF-1 可参与骨组织的多种生理学过程，参与机体的牵引成骨过程；SDF-1 结合软骨组织表面的趋化因子受体，刺激基质金属蛋白酶的释放，从而诱导关节软骨破坏[12]。IL-1 是由单核细胞、巨噬细胞、表皮细胞等合成分泌，包括 IL-1α、IL-1β 等，IL-1β 是一种白细胞介素，可提高机体对疼痛的敏感性[13]。有研究[14]显示：IL-1 可促使退变椎间盘组织合成和分泌 MMP3，从而降解椎间盘间质，腰椎间盘突出患者血清 IL-1β 水平显著高于健康人群。MMP3 是一个重要的金属蛋白酶成员，可降解蛋白多糖聚合体、纤维连接蛋白的作用[15]。已有研究[16]表明 MMP3 水平越高，椎间盘体积缩小越快。然而，血清中上述因子水平与腰椎间盘退变分级的相关性未见报道。本研究结果显示：LDH 患者血清中 SDF-1、MMP3、IL-1β 水平高于健康对照组，这是因为：LDH 患者由于神经根受压产生不适，机体为避免不适则倾向于长时间保持同一种特殊姿势，相应部位肌肉与组织受压或拉伸，导致肌肉受到损伤，同时发生炎性反应；加之 LDH 会导致局部组织出现微循环障碍，缺氧代谢产物堆积，增加细

胞通透性,从而促进SDF-1、MMP3、IL-1β释放入血。

本研究对比不同椎间盘退变程度患者血清中SDF-1、MMP3、IL-1β水平,结果发现:椎间盘突出症患者各亚组血清中SDF-1、MMP3、IL-1β水平随着病变程度增加而升高。进一步进行Spearman相关性分析,结果显示:血清SDF-1、MMP3、IL-1β水平与L4/5、L5/S1节段腰椎间盘分级均呈正相关,表明随着Pfirriman分级增加,LDH患者血清SDF-1、MMP3、IL-1β水平不断升高。这可能是因为,氧化应激、炎症因子、金属蛋白酶等均参与椎间盘退变,过量的MMP3可削弱纤维环的保护作用,MMP3可加速椎间盘的退变,随着椎间盘退变程度加重,椎间盘体积不断缩小,炎性反应程度加剧[17]。

综上所述,血清SDF-1、MMP3、IL-1β表达水平与腰椎间盘退变程度呈正相关,随着病情加重,其表达水平升高,提示血清血清SDF-1、MMP3、IL-1β水平与腰椎间盘退变的发生发展有一定关系。

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