

# 腰椎间盘突出症伴疼痛患者血清细胞因子的改变\*

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**摘要:**目的 研究腰椎间盘突出症患者疼痛与血清细胞因子变化的关系,并讨论其临床意义。方法 选择解放军323医院2014年1月~2016年12月确诊的腰椎间盘突出症患者74例,男性45例,女性29例,年龄 $46.2 \pm 16.1$ 岁,病程 $22.6 \pm 7.8$ 个月。根据VAS疼痛评分为轻度37例,中度23例和重度14例。对照选择同期健康体检者30例,男性18例,女性12例,年龄 $45.3 \pm 15.8$ 岁。全部研究对象于空腹抽取静脉血,采用放射免疫法测定丙二醛(MDA)、超氧化物歧化酶(SOD)、白细胞介素-6(IL-6)、肿瘤坏死因子(TNF),血栓素(TX)、内皮素(ET)、前列腺素E(PGE)和降钙素(CA)水平。结果 与正常对照比较,腰椎间盘突出症血清细胞因子MDA, SOD, IL-6, TNF, TX, ET, PGE和CA均有不同程度升高( $P < 0.05 \sim 0.01$ )。VAS评估腰椎间盘突出症重度疼痛者明显高于中度或轻度疼痛( $P < 0.05 \sim 0.01$ )。经Logistic分析,这些血清细胞因子与腰椎间盘突出症疼痛密切相关( $OR = 2.415 \sim 4.127, 95\%CI = 1.146 \sim 11.735, P < 0.05$ )。结论 腰椎间盘突出症患者多项血清细胞因子与其疼痛程度存在密切关系,提示血清中这些细胞因子在疼痛过程可能影响机体生化代谢。

**关键词:**腰椎间盘突出症;疼痛;血清;细胞因子

中图分类号:R441.1;R446.1 文献标志码:A 文章编号:1671-7414(2018)02-019-04

doi:10.3969/j.issn.1671-7414.2018.02.007

## Changes of Serum Cytokines in Patients with Lumbar Intervertebral Disc Herniation and Pain

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**Abstract:** Objective To study the relationship between the pain of the patients with lumbar intervertebral disc herniation (LIDH) and the changes of serum cytokine, and to discuss the clinical significance. **Methods** From January 2014 to December 2016, 74 cases of LIDH diagnosed in the 323rd Hospital of the PLA were selected, including 45 males and 29 females, whose age was  $46.2 \pm 16.1$  years, and the duration  $22.6 \pm 7.8$  months. According to the VAS pain score, 37 cases were mild, 23 cases were moderate and 14 cases were severe. The control was 30 cases of healthy physical examination in the same period, 18 males and 12 females, age  $45.3 \pm 15.8$  years. All subjects were collected for venous blood on fasting. MDA, superoxide dismutase (SOD), interleukin -6 (IL-6), tumor necrosis factor (TNF), thromboxane (TX), endothelin (ET), prostaglandin E (PGE) and calcitonin (CA) were all measured by radioimmunoassay. The results were analyzed statistically. **Results** The compared with normal control group, serum cytokines MDA, SOD, IL-6, TNF, TX, ET, PGE and CA increased in different degrees ( $P < 0.05 \sim 0.01$ ). The VAS assessment of severe pain in LIDH was significantly higher than that of moderate or mild pain ( $P < 0.05 \sim 0.01$ ). Logistic analysis showed that these serum cytokines were closely related to the pain of LIDH ( $OR = 2.415 \sim 4.127, 95\%CI = 1.146 \sim 11.735, P < 0.05$ ). **Conclusion** The serum cytokines in patients with LIDH are closely related to the degree of pain, suggesting that these cytokines in serum may affect biochemical metabolism in the process of pain.

**Keywords:** lumbar intervertebral disc herniation; pain; serum; cytokine

腰椎间盘突出症(lumbar intervertebral disc herniation, LIDH)是腰部最常见疾病,由于脊髓髓核、纤维环及软骨板的退行性改变,加上外力作用

致使椎间盘纤维环破裂,髓核组织从破裂处脱出或突出到后方或椎管内,相邻脊神经根在刺激或压迫作用下引起局部或伴随相应部位疼痛或活动受限

\* 基金项目:国家自然科学基金(N0.30770670)。

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等临床症状<sup>[1~3]</sup>。腰椎间盘突出症最常发生于腰4~5和腰5~骶1,其发病率超过90%<sup>[4]</sup>。腰椎间盘突出症最明显的症状是疼痛,而疼痛与细胞因子(cytokine)相关的研究较少<sup>[5~7]</sup>。本文研究腰椎间盘突出症患者血清中细胞因子变化与其疼痛的相关性,并讨论这些因子在疾病发生发展中的作用,为研究疾病机制提供参考。

## 1 材料与方法

1.1 研究对象 选择收治于解放军第323医院2014年1月~2016年12月确诊的腰椎间盘突出症伴疼痛患者74例,男性45例,女性29例,年龄19~66(46.2±16.1)岁,病程0.5~139.5(22.6±7.8)个月。全部患者均经CT或MR确诊,并排除心脑血管性疾病、代谢性疾病和肿瘤等疾病。根据腰椎间盘突出症病理改变分为:膨出型(Bulging)26例,突出型(Protrusion)16例,脱出型(Extrusion)17例和游离型(Sequestration)15例。根据VAS疼痛评分标准(0~10分),即①无痛(0分)。②轻度(≤3分):有轻微疼痛且能忍受;③中度(4~6分):疼痛并影响睡眠,尚能忍受;④重度(7~10分):渐进性强烈疼痛,疼痛难忍,常影响食欲和睡眠。结果患者包括:轻度疼痛37例,中度疼痛23例和重度疼痛14例。对照选择我院同期健康体检者30例,男性18例,女性12例,年龄20~61(45.3±15.8)岁。患者组与对照组一般资料比较

具有可比性,差异无统计学意义( $P<0.05$ )。

1.3 血清相关细胞因子测定 全部患者于入院次日,对照于体检当日上午7时空腹抽取静脉血离心提取血清并保存于-20℃备用。相关试剂盒由北京福瑞生物工程公司提供。采用放射免疫法(FJ-2008PS全自动 $\gamma$ 放射免疫计数器,西安核仪器厂)测定血清丙二醇(malonic dialdehyde,MDA)、超氧化物歧化酶(superoxide dismutase,SOD)、白细胞介素-6(interleukin-6,IL-6)、肿瘤坏死因子(tumor necrosis factor, TNF)、血栓素(thromboxane, TX)、内皮素(endothelin, ET)、前列腺素E(prostaglandin E, PGE)和降钙素(calcitonin, CA)含量。

1.4 统计学分析 用软件SPSS17.0进行统计学分析。数据用均数±标准差( $\bar{x}\pm s$ )表示,用 $t$ 检验分析年龄、血清细胞因子等计量资料,检验结果与疾病疼痛的关系用Logistic分析。 $P<0.05$ 即认为有差异具有统计学意义。

## 2 结果

2.1 腰椎间盘突出症血清细胞因子变化 见表1、表2。与正常对照比较,腰椎间盘突出症血清细胞因子MDA, SOD, IL-6, TNF, TX, ET, PGE和CA均有不同程度升高,差异均有统计学意义( $P<0.05\sim0.01$ )。VAS评估腰椎间盘突出症重度疼痛明显高于中度或轻度疼痛者,差异有统计学意义( $P<0.05\sim0.01$ )。

表1 腰椎间盘突出症患者血清MDA, SOD, IL-6, TNF, TX, ET, PGE和CA水平的变化( $\bar{x}\pm s$ )

项 目	对照组( $n=30$ )	患者组( $n=74$ )	轻度疼痛( $n=33$ )	中度疼痛( $n=30$ )	重度疼痛( $n=11$ )	F值	P值
MDA( $\mu\text{mol/L}$ )	4.8±1.2	8.4±1.8	5.1±1.5	7.3±2.3	7.9±1.7	3.679	<0.01
SOD(nU/mg)	103±26	149±22	131±24	148±23	184±25	4.023	<0.01
IL-6(kU/L)	61±17	77±16	71±15	85±19	93±23	3.798	<0.01
TNF(ng/L)	1.5±0.4	1.9±0.5	1.6±0.4	1.9±0.6	2.3±0.6	4.258	<0.01
TX( $\mu\text{g/L}$ )	2 124±872	2 291±761	1 998±816	2 747±719	2 854±887	2.926	<0.01
ET(mg/L)	33.2±9.9	45.9±4.7	36.4±9.6	39.1±3.4	48.2±4.8	4.692	<0.01
PGE( $\mu\text{g/L}$ )	298±191	465±127	426±119	477±172	488±191	3.987	<0.01
CA(ng/L)	28.7±14.3	48.2±13.1	39.2±18.3	44.3±17.6	63.8±16.2	2.917	<0.01

表2 腰椎间盘突出症患者血清MDA, SOD, IL-6, TNF, TX, ET, PGE和CA水平变化比较结果

项 目	患者组与对照组比较		中度疼痛组与对照组比较		重度疼痛与轻度疼痛比较	
	$t$	$P$	$t$	$P$	$t$	$P$
MDA	3.479	<0.01	2.102	<0.05	2.983	<0.01
SOD	3.041	<0.01	2.013	<0.05	3.064	<0.01
IL-6	3.092	<0.01	0.879	>0.05	3.472	<0.01
TNF	2.842	<0.01	1.987	<0.05	2.983	<0.01
TX	2.641	<0.05	2.679	<0.05	3.209	<0.01
ET	3.923	<0.01	0.173	>0.05	2.913	<0.01
PGE	4.876	<0.01	0.892	>0.05	2.818	<0.01
CA	4.937	<0.01	0.192	>0.05	3.622	<0.01

## 2.2 血清细胞因子含量与腰椎间盘突出疼痛关系

见表3。经 Logistic 分析表明,血清细胞因子 MDA, SOD, IL-6, TNF, TX, ET, PGE 和 CA 与腰椎间盘突出症患者疼痛密切相关, ( $P < 0.05$ )。

表3 血清细胞因子与腰椎间盘突出疼痛相关性分析

项 目	WALD值	P值	OR值	95%CI
丙二醇(MDA)	4.422	<0.05	2.415	1.146~6.515
超氧化物歧化酶(SOD)	5.883	<0.05	3.766	1.335~9.875
白细胞介素-6(IL-6)	6.745	<0.05	2.662	1.228~7.108
肿瘤坏死因子(TNF)	4.986	<0.05	4.284	1.341~11.735
血栓素(TX)	5.833	<0.05	2.508	1.194~6.803
内皮素(ET)	5.964	<0.05	2.845	1.234~7.722
前列腺素(EPGE)	6.227	<0.05	2.961	1.281~8.416
降钙素(CA)	6.475	<0.05	4.127	1.315~9.381

3 讨论 腰椎间盘突出症患者血清 MDA, SOD, IL-6, TNF, TX, ET, PGE 和 CA 均有不同程度升高, 且与疼痛程度有一定关系, 提示血清中这些细胞因子在疼痛过程可能影响机体生化代谢, 其机理有待进一步探讨。本文的这一研究结果与既往有关报道相似<sup>[6~8]</sup>。

腰椎间盘突出症是椎间盘的一种退行性病变。临床证实, 纤维环发生退变的同时将影响椎间盘, 并逐渐膨出和突出。髓核是大分子结构的蛋白多糖, 其电荷密度高, 当内部呈现高渗透压时髓核组织内的蛋白多糖则可能发生改变, 并互为因果而影响病变进程<sup>[9,10]</sup>。疼痛的发生是椎间盘纤维环破裂, 其髓核连同残存的纤维环和覆盖其上的后纵韧带向椎管内突出, 压迫邻近的脊神经根或脊髓所产生。这种疼痛多数是压迫后受刺激引起, 其中与亚硝酸胺、炎症与创伤, 或遗传因素有一定关系。大多数腰椎间盘突出症预后较好, 但生活质量却明显降低<sup>[3,9~11]</sup>。手术减压是治疗腰椎间盘突出症疼痛的根本, 但应根据椎间盘突出位置、范围及对神经压迫程度, 以及是否存在椎管狭窄等个体化病情来处理<sup>[7~9]</sup>。

细胞因子中的促炎因子可以参与全身炎症反应, 其中的 IL-6 是影响最大的介质, 它对中枢神经系统的多种受体和离子通道, 如钠离子通道、GABA 受体等均有重要的作用<sup>[7,12~14]</sup>。同时还能协同其他介质以清除自由基, 抑制脂质过氧化反应, 还原高氧化态铁蛋白和调节钙离子平衡等作用, 特别是在降低组织氧耗和增加组织对缺氧的耐受性方面的作用更为明显<sup>[13~15]</sup>。当组织缺血-再灌注发生时, 细胞因子则出现分泌改变从而降低应激和炎症反应, 以降低组织细胞损伤<sup>[8~11,16]</sup>。腰椎间盘突出症疼痛加重时, 促炎症细胞因子可能大量释放, 这些因子的释放与局部组织损害密切相关。此

外, 细胞因子促炎性反应表达受到抑制时, 其核转录因子 NF- $\kappa$ B(核因子- $\kappa$ B)的表达可以受到抑制或减弱, 从而使细胞形成自我保护<sup>[15~18]</sup>。

目前对腰椎间盘突出症疼痛相关的治疗与诊断研究较多<sup>[13~15]</sup>, 但患者关节性和神经性疼痛与细胞因子变化的研究则相对较少, 其研究指标和结果差异比较大<sup>[16~18]</sup>, 对其病理机制的解释也不一定合适<sup>[3~5]</sup>。临床疼痛相关的神经肽类指标较多, 研究比较多的是物质 P(SP)和神经肽 Y(NPY), 它们与神经性疼痛密切相关<sup>[5,6]</sup>。腰椎间盘突出症伴随的疼痛与白介素、TNF- $\alpha$ , SP, NPY 和基质金属蛋白酶(MMP)水平变化有一定关联已被一些研究证实, 对其病理生理的深入了解有一定参考意义<sup>[19]</sup>。

本文对腰椎间盘突出症患者血清多项细胞因子与其疼痛程度进行相关性分析, 结果表明腰椎间盘突出症血清 MDA, SOD, IL-6, TNF, TX, ET, PGE 和 CA 水平均较健康对照明显升高, 同时与疼痛程度有一定相关性, 疼痛严重者其水平越高。Logistic 分析提示, 这些指标与腰椎间盘突出症疼痛存在密切关联, 对这些血清指标的检测或许可以作为本病监测的参考。这些指标的变化可能是疾病引起炎症和局部组织损伤引起, 而炎症引起的疼痛作为一种神经性疼痛, 反过来又导致细胞因子水平的变化, 从而形成恶性循环。

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收稿日期: 2017-12-17

修回日期: 2018-01-05

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收稿日期: 2017-12-13

修回日期: 2018-01-31