·基础研究·

脂氧素 A_4 对椎间盘突出所致大鼠根性神经痛的影响

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【摘　要】 **目的**　观察脂氧素 A_4 对椎间盘突出所致大鼠根性神经痛的影响。**方法**　选取雄性 SD 大鼠 48 只，建立非压迫性椎间盘突出模型，按照随机数字表法将其分为假手术组（假手术 + 10 μl 生理盐水）、对照组（模型 + 10 μl 生理盐水）、脂氧素 A_4 10 ng 组（模型 + 10 ng 脂氧素 A_4）、脂氧素 A_4 100 ng 组（模型 + 100 ng 脂氧素 A_4），每组 12 只。手术当天及术后连续 3 d 鞘内注射脂氧素 A_4 或生理盐水，观察大鼠的行为学变化，并测定 50% 缩足阈值（50% PWT）。术后 7 d 取大鼠术侧腰段脊髓背角，用 Western blot 法测定 c-Jun 氨基末端激酶（JNK）、细胞外信号调节激酶（ERK）的蛋白表达量，并用 ELISA 技术测定肿瘤坏死因子 α（TNF-α）、白细胞介素 1β（IL-1β）和转化生长因子-β1（TGF-β1）的含量。**结果**　假手术组 50% PWT 在手术前后无显著变化（$P>0.05$）。与组内术前比较，对照组和脂氧素 A_4 10 ng 组术后各时间点的 50% PWT 降低（$P<0.05$）。与假手术组术后同时间点比较，对照组和脂氧素 A_4 10 ng 组术后各时间点的 50% PWT 较低（$P<0.05$）。与对照组比较，脂氧素 A_4 10 ng 组术后 3 d［(8.90 ± 2.76) g］、5 d［(8.56 ± 2.77) g］的 50% PWT 较高（$P<0.05$）。脂氧素 A_4 100 ng 组术后 2 d、3 d、4 d、5 d、6 d、7 d 的 50% PWT 显著较高（$P<0.05$）。与假手术组比较，对照组、脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组 p-JNK、p-ERK 水平明显升高（$P<0.05$）。与对照组比较，脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组 p-JNK、p-ERK 水平明显降低（$P<0.05$），且脂氧素 A_4 100 ng 组下降更明显（$P<0.05$），呈剂量依赖性。各组 t-JNK 和 t-ERK 蛋白含量之间比较，差异无统计学意义（$P>0.05$）。与假手术组比较，对照组、脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组 TNF-α、IL-1β 的表达水平明显升高，TGF-β1 的表达水平明显降低（$P<0.05$）。与对照组比较，脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组 TNF-α、IL-1β 的表达水平明显降低（$P<0.05$），TGF-β1 的表达水平明显升高（$P<0.05$），且脂氧素 A_4 100 ng 组的变化更明显，呈剂量依赖性。**结论**　脂氧素 A_4 能够减轻非压迫性椎间盘突出大鼠的根性神经痛，其机制可能与抑制 ERK 和 JNK 活性、下调促炎因子表达水平、上调抗炎因子表达水平有关。

【关键词】 脂氧素 A_4；　椎间盘突出；　炎症；　根性神经痛

The effect of lipoxin A_4 on radicular pain caused by intervertebral disc herniation

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【**Abstract**】 **Objective**　To investigate the effect of lipoxin A_4 (LXA_4) on radicular pain caused by intervertebral disc herniation. **Methods**　Non-compressive intervertebral disc herniation was induced into forty-eight adult male Sprague-Dawley rats, and they were divided into a sham group (sham operation + 10 μl normal saline), a control group (modeled + 10 μl normal saline), an LXA_4 10 ng group (modeled + 10 ng LXA_4) and an LXA_4 100 ng group (modeled + 100 ng LXA_4), with 12 rats in each group. The normal saline (10 μl) or LXA_4 (10 μl) was administered intrathecally right after the operation and on each of the three succeeding days. General behavior was observed and the 50% paw withdrawal threshold (50% PWT) was measured. On postoperative day 7 all the rats were killed and the ipsilateral lumbar (L_{4-6}) segments of their spinal dorsal horns were removed for determination of the expression of p-JNK, t-JNK, p-ERK and t-ERK proteins using western blotting. TNF-α, IL-1β and TGF-β1 expression were determined using ELISA. **Results**　There was no significant difference in the 50%

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PWT of the sham group before and after surgery, but the 50% PWTs of the control group and the LXA_4 10 ng group were significantly decreased after the operation compared with their values beforehand and significantly lower than the value of the sham group at all time points. Moreover, the 50% PWT of the LXA_4 10 ng group on postoperative days 3 and 5 was significantly higher than the control group; as was the value of the LXA_4 100 ng group on postoperative days 2, 3, 4, 5, 6 and 7. The p-JNK and p-ERK expression in the control group, the LXA_4 10 ng group and the LXA_4 100 ng group were all increased significantly more than in the sham group, but their expression in the LXA_4 10 ng group and LXA_4 100 ng group were decreased significantly more in a dose-dependent manner compared with the control group, with the LXA_4 100 ng group showing the greatest decrease. There were no significant differences in t-JNK or t-ERK expression within each group. **Conclusion** LXA_4 can alleviate radicular pain caused by non-compressive lumbar intervertebral disc herniation. The underlying mechanism involves inhibiting the activation of the ERK and JNK pathways, reducing the expression of pro-inflammatory cytokines and increasing the expression of anti-inflammatory cytokines.

【**Key words**】 Lipoxin A_4; Intervertebral disc herniation; Inflammation; Radicular pain

根性神经痛是椎间盘突出症的常见症状之一,疼痛剧烈,迁延难愈。研究表明,除机械压迫因素外,突出的髓核(nucleus pulposus,NP)组织诱发的炎症反应是根性神经痛的重要原因之一[1]。脂氧素是体内重要的内源性促炎症消退介质,是炎症反应的主要“刹车信号”之一,其是花生四烯酸在脂加氧酶的作用下通过跨细胞途径合成的,对多种炎症细胞和炎症因子有显著的负性调节作用[2]。目前,脂氧素促进炎症消退的作用已在急性肺损伤、哮喘、肾纤维化等疾病中得到证实,有关其对椎间盘突出所致根性神经痛影响的研究尚较为少见。本研究通过建立非压迫性椎间盘突出症大鼠模型,采用鞘内给药方式观察脂氧素 A_4 对椎间盘突出所致大鼠根性神经痛的影响,旨在为脂氧素治疗根性神经痛的临床应用提供基础实验依据。

材料与方法

一、实验仪器和试剂

主要实验仪器包括:Spectra Max M2 型 ELISA 酶标仪(美国产)、LAS-4000 型化学发光成像分析仪(日本产)。主要试剂包括:脂氧素 A_4(美国产),肿瘤坏死因子 α(tumor necrosis factor-α,TNF-α)、白细胞介素 1β(interleukin 1beta,IL-1β)、转化生长因子-β1(transforming growth factor-β1,TGF-β1)ELISA 试剂盒均产自河北博海生物工程开发公司,兔抗鼠 c-Jun 氨基末端激酶(c-Jun amino-terminal kinase,JNK)一抗(美国产),兔抗鼠 p-JNK 一抗(美国产),兔抗鼠细胞外信号调节激酶(extracellular-signal regulated protein kinase,ERK)一抗(美国产),兔抗鼠 p-ERK 一抗(美国产),羊抗兔生物素化二抗(武汉产)。

二、实验动物及分组

选取成年 Sprague-Dawley(SD)雄性大鼠 48 只,体重 250 ~ 300 g,由山东大学动物实验中心提供,安静环境分笼饲养,室温(23 ± 2)℃,维持大鼠 12 h/12 h 昼夜节律(每日 8:00 ~ 20:00 光照)。本研究严格遵守山东大学动物保护和使用规定,按照随机数字表法将大鼠分为假手术组、对照组、脂氧素 A_4 10 ng 组、脂氧素 A_4 100 ng 组,每组 12 只。

三、模型建立

1. 鞘内给药方法:参照 Yaksh 等[3]的方法,采用 10% 水合氯醛(0.3 ml/0.1 kg)腹腔麻醉大鼠后暴露寰枕膜,用 PE-10 号导管置入,脑脊液沿导管涌出视为置管成功,固定导管并缝合伤口。术后大鼠单笼饲养,剔除出现运动功能障碍的大鼠,沿导管注射 2% 利多卡因 10 μl,注射 30 s 后大鼠双后肢麻痹,表示置管位置正确。

2. 非压迫性椎间盘突出模型:参照 Kim 等[4]的方法,将大鼠麻醉后,在两髂嵴连线中点做 25 ~ 30 mm 的正中纵切口,行右侧 L_5 下关节突、L_6 上关节突和 L_5 半椎板切除术,暴露 L_5 背根神经节(dorsal root ganglion,DRG)及部分脊髓硬膜囊。在鼠尾近根部行纵切口,分离显露 2 个椎间隙,切开 2 个纤维环,取出自体髓核组织(约 0.4 mg),将取出的自体髓核组织覆盖于右侧 L_5 DRG 及附近硬膜外腔。假手术组仅暴露相应手术部位而不做其它处理。

四、治疗方法

造模成功后,假手术组和对照组大鼠分别注射 10 μl生理盐水,脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组大鼠分别注射脂氧素 A_4 10 ng 和 100 ng。

五、检测指标

术前 1 d 及术后 7 d,连续观察大鼠行为学变化并测定术侧 50% 缩足阈值(50% paw withdrawal threshold,50% PWT),然后处死大鼠,取术侧脊髓背角测定相关信号通路及炎性因子的变化水平。

1. 行为学观察:将大鼠放置于有机玻璃箱内,观察大鼠有无烦躁、撕咬肢体、运动功能障碍及大小便失禁等情况。

2. 50% PWT 测定：根据 Chaplan 等[5] 报道的方法检测 50% PWT。将大鼠置于透明有机玻璃箱内，自由活动，安静后以不同折力的 von Frey 纤毛机械刺激针（美国产）刺激大鼠足底，避开肉垫使之稍成“S”形，持续6 ~ 8 s。大鼠后肢迅速畏缩、撤回，视为阳性反应。当力度刺激不能引起阳性反应时，则给予相邻高级别力度的刺激；若出现阳性反应，则给予相邻低级别力度的刺激，如此连续进行，每个强度反复刺激 5 次，将出现 3 次以上阳性反应的最小强度定为大鼠的 50% PWT，其单位以压力（g）表示，两次刺激之间至少间隔约 15 s。

3. JNK、ERK 蛋白含量测定：术后 7 d，采用水合氯醛腹腔麻醉大鼠后处死，取术侧 L_{4-6} 段脊髓背角，低温下研磨提取蛋白，加入蛋白裂解液，离心后取上清液，测定蛋白浓度。将提取的蛋白等量加样（40 μg），进行十二烷基磺酸钠（sodium dodecyl sulfate，SDS）-聚丙烯酰胺凝胶电泳（polyacrylamide gelelectrophoresis，PAGE），然后将凝胶中的蛋白转移到电转膜上。电转完毕后，将电转膜置于 5% 的脱脂奶粉中封闭 1 h，加入一抗 4 ℃摇床孵育过夜，洗膜 3 次，再加入二抗摇床孵育 1 h，洗膜 3 次，最后用发光试剂盒显像。所得结果经扫描后用 Quantity one v4.62 版软件计算灰度值，并以假手术组的平均值作为正常值，计算相对灰度值，观察 p-JNK、t-JNK、p-ERK 和 t-ERK 蛋白的表达水平。

4. 促炎因子和抗炎因子测定：测定肿瘤坏死因子 α（tumor necrosis factor-α，TNF-α）、白细胞介素 1β（interleukin 1beta，IL-1β）、转化生长因子-β1（transforming growth factor-β1，TGF-β1）的含量。取术侧 L_{4-6} 段脊髓背角，按重量体积比加入预冷生理盐水作匀浆介质，在冰水混合物条件下用 1 ml 旋转匀浆器制成 10% 的组织匀浆，离心取上清液。严格按照 TNF-α、IL-1β 和 TGF-β1 ELISA 试剂盒说明书进行操作，将标准品浓度和样品对应的吸光度值绘制成标准曲线，计算各细胞因子的含量。

六、统计学分析

采用 SPSS 19.0 版统计学软件进行数据分析，计量资料以（$\bar{x} \pm s$）形式表示，组间比较采用单因素方差分析，两两比较采用邦弗朗尼（Bonferroni）事后检定/检验法，$P < 0.05$ 表示差异有统计学意义。

结　果

一、行为学观察结果

术后各组大鼠精神状态良好，对照组大鼠出现右侧足底轻度外翻、右后肢畏惧着地等疼痛敏感体征，无自噬肢体和运动功能障碍等状况。

二、各组大鼠不同时间点术侧 50% PWT 变化情况

术前各组大鼠术侧 50% PWT 之间比较，差异无统计学意义（$P > 0.05$）。假手术组 50% PWT 在手术前后无显著变化（$P > 0.05$）。与组内术前比较，对照组和脂氧素 A_4 10 ng 组术后各时间点的 50% PWT 降低，差异有统计学意义（$P < 0.05$）。与假手术组术后同时间点比较，对照组和脂氧素 A_4 10 ng 组术后各时间点的 50% PWT 较低，差异有统计学意义（$P < 0.05$）。与对照组比较，脂氧素 A_4 10 ng 组术后 3 d、5 d 的 50% PWT 较高，差异有统计学意义（$P < 0.05$）。与对照组术后同时间点比较，脂氧素 A_4 100 ng 组术后 2 d、3 d、4 d、5 d、6 d、7 d 的 50% PWT 显著较高，差异有统计学意义（$P < 0.05$），详见表 1。

三、各组大鼠术后 7 d p-JNK、t-JNK、p-ERK、t-ERK 蛋白的表达情况

以甘油醛-3-磷酸脱氢酶（glyceraldehyde-3-phosphate dehydrogenase，GAPDH）作为参考。与假手术组比较，对照组、脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组 p-JNK、p-ERK 水平明显升高，差异有统计学意义（$P < 0.05$）。与对照组比较，脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组 p-JNK、p-ERK 水平明显降低，差异有统计学意义（$P < 0.05$），且脂氧素 A_4 100 ng 组下降更明显（$P < 0.05$），呈剂量依赖性。各组 t-JNK 和 t-ERK蛋白含量之间比较，差异无统计学意义（$P > 0.05$），详见图 1。

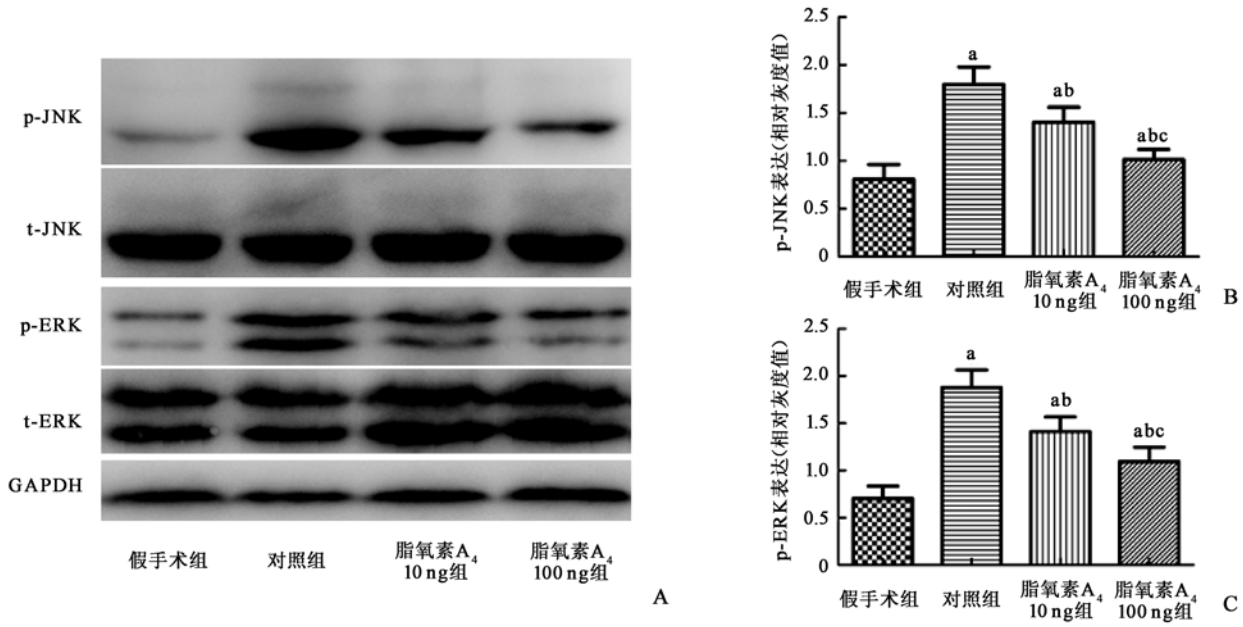
四、各组大鼠术后 7 d 术侧脊髓背角 TNF-α、IL-1β、TGF-β1 的表达水平

与假手术组比较，对照组、脂氧素 A_4 10 ng 组和脂氧素 A_4 100 ng 组 TNF-α、IL-1β 的表达水平明显升高，TGF-β1 的表达水平明显降低，差异有统计学意义（$P < 0.05$）。与对照组比较，脂氧素 A_4 10 ng 组和脂

表 1　各组大鼠不同时间点术侧 50% PWT 变化情况（g，$\bar{x} \pm s$）

组别	例数	术前	术后 1 d	术后 2 d	术后 3 d	术后 4 d	术后 5 d	术后 6 d	术后 7 d
假手术组	12	14.85 ± 2.40	13.84 ± 1.92	14.83 ± 2.03	14.76 ± 1.94	14.53 ± 1.84	14.25 ± 1.99	14.52 ± 1.69	14.63 ± 1.97
对照组	12	15.09 ± 1.93	7.20 ± 1.52^{ab}	5.99 ± 2.02^{ab}	4.89 ± 1.80^{ab}	4.71 ± 2.61^{ab}	4.25 ± 1.70^{ab}	4.31 ± 2.15^{ab}	3.48 ± 1.62^{ab}
脂氧素 A_4 10 ng 组	12	14.30 ± 1.97	8.73 ± 3.63^{ab}	8.59 ± 2.65^{ab}	8.90 ± 2.76^{abc}	8.69 ± 3.41^{ab}	8.56 ± 2.77^{abc}	8.05 ± 2.73^{ab}	7.74 ± 2.75^{ab}
脂氧素 A_4 100 ng 组	12	14.62 ± 1.77	11.13 ± 2.11	11.24 ± 3.35^{c}	11.93 ± 2.65^{c}	11.39 ± 2.50^{c}	11.19 ± 3.35^{c}	10.95 ± 2.71^{c}	10.64 ± 3.68^{c}

注：与组内术前比较，$^{a}P < 0.05$；与假手术组术后同时间点比较，$^{b}P < 0.05$；与对照组术后同时间点比较，$^{c}P < 0.05$



注：与假手术组比较，$^{a}P<0.05$；与对照组比较，$^{b}P<0.05$；与脂氧素 A_4 10 ng 组比较，$^{c}P<0.05$；其中，图 A 为各组大鼠术后 7 d p-JNK、t-JNK、p-ERK、t-ERK 蛋白电泳图，图 B 为术后 7 d 各组大鼠 p-JNK 蛋白的表达情况，图 C 为术后 7 d 各组大鼠 p-ERK 蛋白的表达情况

图 1　术后 7 d 大鼠术侧脊髓背角丝裂原活化蛋白激酶通路中 p-JNK、t-JNK、p-ERK、t-ERK 的蛋白含量

氧素 A_4 100 ng 组 TNF-α、IL-1β 的表达水平明显降低，TGF-β1 的表达水平明显升高，差异有统计学意义（$P<0.05$），且脂氧素 A_4 100 ng 组的变化更明显（$P<0.05$），呈剂量依赖性，详见表 2。

表 2　各组大鼠术后 7 d 术侧脊髓背角 TNF-α、IL-1β、TGF-β1 的表达水平（pg/mg，$\bar{x}\pm s$）

组别	例数	TNF-α	IL-1β	TGF-β1
假手术组	6	58.22 ± 18.77	28.98 ± 9.28	179.33 ± 15.81
对照组	6	289.62 ± 33.04^{a}	132.13 ± 13.20^{a}	61.23 ± 13.32^{a}
脂氧素 A_4 10 ng 组	6	200.49 ± 24.15^{ab}	70.76 ± 16.33^{ab}	85.99 ± 20.59^{a}
脂氧素 A_4 100 ng 组	6	141.92 ± 23.22^{abc}	55.86 ± 10.32^{ab}	123.81 ± 20.92^{abc}

注：与假手术组比较，$^{a}P<0.05$；与对照组比较，$^{b}P<0.05$；与脂氧素 A_4 10 ng 组比较，$^{c}P<0.05$

讨　论

本研究中，大鼠建模后表现为自发抬起患肢、患侧足底轻度外翻、患肢着地时间较健侧明显缩短且其术侧机械痛阈显著下降，提示出现机械痛敏。髓核组织的致炎特性是非压迫性腰椎间盘突出所致根性神经痛的重要机制之一[1]。根据免疫学家 Bumet 的克隆选择学说，髓核作为“隔离抗原”存在于机体内，一旦突出、暴露于免疫系统，即可激发机体产生自身免疫反应，诱发炎症，促使中性粒细胞、单核巨噬细胞等炎性细胞募集、增殖，释放各种溶酶、炎症细胞因子，引起神经干肿胀、空泡变性，从而导致根性神经痛[6]。

本研究发现，鞘内注射脂氧素 A_4 能明显减轻非压迫性腰椎间盘突出大鼠的 50% PWT。脂氧素是 Serhan 等[7]发现的一类花生四烯酸的代谢产物，是体内重要的内源性脂质抗炎介质之一。脂氧素 A_4 是脂氧素家族中重要的一员，通过与细胞表面高亲和力的 G 蛋白偶联受体——脂氧素受体（receptor for lipoxin A_4，ALXR）结合，从而发挥生物学效应[8]。脂氧素能阻止炎症部位中性粒细胞募集，增强单核细胞和巨噬细胞的吞噬能力，抑制促炎因子的表达水平，提高抗炎因子的表达水平，从而促进炎症消退[9]。近年来，脂氧素促进炎症消退的作用已经在哮喘、关节炎、脑缺血等疾病领域内得到验证[10]。近期，有研究证实脂氧素 A_4 能减轻吗啡诱导痛觉过敏大鼠的炎症反应，下调脊髓背角促炎因子（IL-1β 和 TNF-α）的表达水平，上调抗炎因子（TGF-β1）的表达水平[11]。本课题组在前期研究中也发现脂氧素 A_4 能减轻背根神经节损伤大鼠的痛觉过敏程度，降低背根神经节促炎因子（IL-1β 和 TNF-α）的表达水平[12]。有研究报道，在局部脑缺血再灌注大鼠模型中，脂氧素类似物可通过上调皮质缺血区抗炎因子的表达水平来减轻炎症反应[13]。但另有研究发现，ALXR 激动剂能够下调肝纤维化大鼠模型肝组织 TGF-β1 的表达水平，推测这可能与疾病模型的差异有关，其具体机制尚需进一步研究证实[14]。炎性因子在炎症反应所致痛觉过敏中起到重要作用。研究发现，TNF-α 被认为是触发细胞因子活化的关键因子，鞘内给予 TNF-α 能提高痛觉过敏程度，阻断 TNF-α 后，疼痛过敏程度显著减轻[15]。IL-1β 也被证

实在诱导神经病理性疼痛中起到重要作用,鞘内给予 IL-1β 受体拮抗剂能明显降低病理性神经痛大鼠模型的机械痛阈[16]。TGF-β1 是重要的抗炎因子,研究发现,慢性压迫性损伤(chronic constrictive injury, CCI)大鼠术侧脊髓背角 TGF-β1 含量明显降低,而在鞘内给予外源性 TGF-β1 后能明显降低 CCI 大鼠的热痛阈[17]。也有研究证实,鞘内给予外源性 TGF-β1 能减轻部分坐骨神经结扎大鼠模型的神经病理性疼痛[18]。因此,本研究推测脂氧素 A_4 可能是通过降低促炎因子水平、提高抗炎因子水平来减轻非压迫性椎间盘突出大鼠的根性神经痛。

JNK 和 ERK 是丝裂原活化蛋白激酶家族中的重要成员,在调节组织及神经损伤导致的疼痛敏化状态方面具有显著作用[19]。研究发现,脊髓星形胶质细胞 ERK 活性对于稳定慢性疼痛程度具有重要作用,鞘内给予 ERK 抑制剂能够显著抑制脊神经结扎大鼠的机械痛觉过敏[20]。持续激活脊髓星形胶质细胞 JNK 可诱发持久的病理性神经痛,鞘内给予 JNK 抑制剂能减轻脊神经结扎大鼠的病理性神经痛[21]。有研究证实,脂氧素 A_4 与脊髓星形胶质细胞上的 ALXR 结合后,发挥镇痛作用是通过抑制促分裂素原活化蛋白激酶(mitogen-activated protein kinases, MAPK)信号通路激活而得以实现[22]。脂氧素 A_4 能够抑制小鼠脑组织 p-ERK 和 p-JNK 活性,从而减轻创伤性脑损伤小鼠的脑部损伤程度[23]。本研究证实,鞘内给予脂氧素 A_4 能明显抑制非压迫性椎间盘突出大鼠脊髓背角 p-ERK 和p-JNK的活性,提示脂氧素 A_4 减轻非压迫性椎间盘突出症大鼠的根性神经痛可能与抑制脊髓背角 ERK 和 JNK 的活性有关。另外有研究证实,炎性因子能激活 ERK 和 JNK[24-25],而其被激活后能进一步促进炎性因子释放,形成正反馈调节,从而扩大炎症范围[26-27]。

综上所述,脂氧素 A_4 能够明显减轻非压迫性椎间盘突出症大鼠的根性神经痛,其机制可能与抑制 ERK 和 JNK 活性、下调促炎因子表达水平、上调抗炎因子表达水平有关。

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·外刊撷英·

Chondroprotection and prevention of osteoarthritis progression

BACKGROUND AND OBJECTIVE Osteoarthritis (OA) is a major cause of musculoskeletal pain and disability worldwide. Most treatment focuses on reducing symptoms, rather than modifying the disease process itself. This systematic literature review was designed to better understand the evidence for the routine use of agents to modify the progression of the OA disease process.

METHODS An initial literature search identified 12 treatment agents, each recognized as possessing potential chondroprotective properties of the joint. The authors then identified randomized, controlled trials with a minimum of 12 months' follow-up, evaluating the efficacy of each of those agents. Measures included joint space width, distance between the femoral condyle and the tibial plateau and joint space narrowing or changes in cartilage volume. Of the articles reviewed, 13 fulfilled the criteria.

RESULTS The data revealed that the long-term use of both oral glucosamine and chondroitin sulfate may have a small, but significant, effect on slowing disease progression in patients with OA of the knee. No conclusions were possible for treatment using intra-articular injections of these agents. Oral vitamins, including D and E, as well as nonsteroidal anti-inflammatory drugs, did not significantly affect the progression of the joint disease.

CONCLUSION This literature review supports the use of both oral glucosamine and chondroitin sulfate as structure modifying, chondroprotective drugs in patients with osteoarthritis of the knee.

【摘自:Gallagher B, Tjoumakaris FP, Harwood MI, et al. Chondroprotection and the prevention of osteoarthritis progression of the knee: a systematic review of treatment agents. Am J Sports Med. 2015, 43(3): 734-744.】

Nsaids: effects on osteoarthritis symptoms and disease progression

BACKGROUND AND OBJECTIVE An estimated 27 million people in the United States have osteoarthritis (OA). Clinical guidelines for the management of this disease include both pharmacologic and nonpharmacologic therapies. This study was designed to estimate the extent to which prescription nonsteroidal anti-inflammatory drugs (NSAIDs), taken over the long-term, affect the symptoms and disease progression of OA.

METHODS Between 2004 and 2006, the Osteoarthritis Initiative (OAI) collected baseline data from four study sites, including a total of 4,796 patients with established OA, or who were at high risk for developing OA of the knee, and were not taking an NSAID at study onset, and who began use during the study period. The participants were evaluated for four years with annual follow-up assessments. All were assessed for changes in the Western Ontario and McMaster University Osteoarthritis Index (WOMAC), as well as for radiographic progression over four years. These outcomes were compared between NSAID users and nonusers.

RESULTS Among nonusers at baseline, six percent initiated treatment by one year, with 52% reporting regular use. Any prescription NSAID reported on the most recent assessment was not associated with scores for pain, stiffness or physical function on the WOMAC or with the joint space width. However, among those reporting use of prescription NSAIDs at all three of the yearly assessments, improvements were noted in patient reports of stiffness and function, with delayed joint space width progression.

CONCLUSION This study found that long-term, but not short-term, use of NSAIDS is associated with important changes in stiffness, physical function and joint space width among patients with osteoarthritis of the knee.

【摘自:Lapane KL, Yang S, Driban JB, et al. Effects of prescription nonsteroidal anti-inflammatory drugs on symptoms and disease progression among patients with knee osteoarthritis. Arthritis Rheumatol. 2015, 67(3): 724-732.】