

# 非布司他联合依托考昔治疗痛风性关节炎的临床疗效分析



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**【摘要】目的** 分析非布司他联合依托考昔治疗痛风性关节炎 (gouty arthritis, GA) 的临床疗效。**方法** 选取 2020 年 4 月至 2022 年 9 月温州医科大学附属第一医院收治的 180 例 GA 患者作为研究对象, 将患者分为对照组、观察组, 每组 90 例。对照组采用依托考昔治疗, 观察组采用非布司他联合依托考昔治疗。为期 1 周的疗程结束后, 比较两组患者的临床疗效、疼痛程度、尿酸 (uric acid, UA)、红细胞沉降率 (erythrocyte sedimentation rate, ESR)、C 反应蛋白 (C reactive protein, CRP) 指标及不良反应。**结果** 一周后, 观察组患者痛风性关节炎临床疗效评价有效率高于对照组 (96.67% vs. 66.67%,  $P < 0.001$ ); 两组患者视觉疼痛模拟评分 (visual pain simulation score, VAS) 均下降, 观察组显著低于对照组 ( $1.18 \pm 0.58$  vs.  $2.67 \pm 0.92$ ,  $P < 0.001$ ); 两组患者尿酸、血沉、C 反应蛋白指标均下降, 观察组显著低于对照组 ( $P < 0.001$ ); 两组患者药物相关不良反应发生率比较, 差异无统计学意义 (23.33% vs. 18.89%,  $P=0.363$ )。**结论** 非布司他联合依托考昔治疗痛风性关节炎有助于改善临床疗效。

**【关键词】** 痛风性关节炎; 非布司他; 依托考昔; 临床疗效; 不良反应

## Analysis of clinical efficacy of febuxostat combined with etoricoxib in the treatment of gouty arthritis

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**【Abstract】Objective** To investigate the clinical efficacy of febuxostat combined with etoricoxib regimen in the treatment of gouty arthritis (GA). **Methods** A total of 180 patients with GA admitted to The First Affiliated Hospital of Wenzhou Medical University from April 2020 to September 2022 were included as the analysis subjects, and the patients were divided

into control group and observation group, with 90 cases in each group. The control group was treated with etoricoxib, and the observation group was treated with febuxostat combined with etoricoxib. After a one-week course of treatment, the two groups of GA patients were compared in terms of clinical efficacy, pain degree, uric acid (UA), erythrocyte sedimentation rate (ESR), C reactive protein (CRP) indexes and adverse reactions. **Results** The clinical efficacy evaluation of gouty arthritis in the observation group was higher than that in the control group (96.67% vs. 66.67%,  $P < 0.001$ ). The visual pain simulation score (VAS) decreased in both groups, and the score of patients in the observation group was significantly lower than that in the control group ( $1.18 \pm 0.58$  vs.  $2.67 \pm 0.92$ ,  $P < 0.001$ ). UA, ESR and CRP indexes decreased in both groups, and the indexes of patients in the observation group were significantly lower than those in the control group ( $P < 0.001$ ). There was no significant difference of drug-related adverse reactions between the two groups (23.33% vs. 18.89%,  $P = 0.363$ ). **Conclusion** Febuxostat combined with etoricoxib has a significant effect in patients with gouty arthritis.

**【Keywords】** Gouty arthritis; Febuxostat; Etoricoxib; Clinical efficacy; Adverse reactions

痛风性关节炎 (gouty arthritis, GA) 指机体长期处于嘌呤代谢异常状态, 软组织沉积大量尿酸结晶并出现以关节疼痛为典型症状的情况。尿酸盐可沉积在患者的关节、韧带、软骨、肌腱等部位, 以足部第一趾关节最为常见。近年来 GA 发病率呈明显升高趋势, 与人们的饮食习惯、作息节奏等有关, 随着病情进展, 关节可出现畸形, 因此 GA 有一定的致残率<sup>[1-3]</sup>。目前对 GA 患者重点在于控制其病情发展。依托考昔可在短期缓解 GA 患者关节疼痛, 但有研究显示其在调整尿酸方面的效果有限, 非布司他为黄嘌呤氧化酶抑制剂, 能够抑制尿酸合成, 有降尿酸效果<sup>[4-5]</sup>。本研究旨在探析依托考昔联合非布司他对于 GA 患者的临床价值及安全性。

## 1 资料与方法

### 1.1 研究对象

选取 2020 年 4 月至 2022 年 9 月温州医科大学附属第一医院收治的 180 例 GA 患者作为研究对象, 将患者分为对照组、观察组, 每组 90 例。纳入标准: ①入院时有严重的关节疼痛, 行尿酸钠晶体检测提示为阳性; ②年龄 18 岁以上; ③进入本研究前 2 周内未服用激素类药物; ④尿酸值检测超过  $420 \mu\text{mol/L}$ 。排除标准: ①合并肝肾等重要脏器器质性病变或心肺等功能异常; ②有严重的关节畸形; ③有精神疾病或认知障碍等。本研究经温州医科大学附属第一医院伦理委员会审核批准 (LWYJ2022-094)。

### 1.2 治疗方法

对照组采用依托考昔片 (杭州默沙东制药有限公司, 生产批号: N028618, 规格为 60 mg/片) 治疗, 口服, 每次 2 片, 每天 1 次, 疗程 1 周。观察组在采用依托考昔片治疗基础上联合非布司他 (商品名: 优立通, 江苏万邦生化医药集团有限责任公司, 生产批号: 1801739, 规格 40 mg/片), 口服, 每次 1 片, 每天 1 次, 疗程 1 周。两组患者均减少疼痛关节的活动, 避免受冷受湿; 低嘌呤饮食, 禁酒; 每天饮水量不低于 2 000 mL 以刺激尿酸排泄。

### 1.3 观察指标

(1) 疗效: 1 个疗程后患者的关节症状如肿胀、疼痛、活动受限等完全消失, 可自由行动为显效; 相关症状缓解, 能够缓慢地自主行动为有效; 相关症状无改善甚至疼痛程度加重为无效<sup>[6]</sup>。

(2) 疼痛: 分别在用药前、疗程后采用视觉疼痛模拟评分 (visual pain simulation score, VAS) 进行评估, 分数在 0~10 分间, 分数越高患者的自觉疼痛感越严重<sup>[7]</sup>。(3) 尿酸 (uric acid, UA)、红细胞沉降率 (erythrocyte sedimentation rate, ESR)、炎症因子: 分别在用药前 (用药当天清晨)、疗程后 (完成疗程后次日清晨) 检测患者 UA、ESR、C 反应蛋白 (C reactive protein, CRP), 其中 UA 检测采用尿酸氧化酶法, 仪器为奥林巴斯 AU400 全自动生化分析仪, 尿酸测定试剂盒来自基蛋生物科技股份有限公司; ESR 采用魏氏法 (Westergren 法); C 反应蛋白检测应用全血快

速C反应蛋白测定仪,试剂盒购自北京北瑞达医药科技有限公司。(4)不良反应:两组患者在1周用药期间内出现肝功能异常、恶心呕吐、腹泻、头痛事件数。

#### 1.4 统计分析

数据采用SPSS 25.0软件分析,正态分布的计量资料(疼痛评分、血清炎症因子)用均数与标准差( $\bar{x} \pm s$ )表示,采用 $t$ 检验;计数资料(临床疗效、不良反应)用频数与百分比( $n, \%$ )表示,采用 $\chi^2$ 检验。以 $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 一般资料

对照组男性52例、女性38例,年龄37~68岁、平均( $48.52 \pm 2.64$ )岁,病程1~5年、平均( $3.85 \pm 0.87$ )年,治疗史2个月至3年、平均( $1.87 \pm 0.25$ )年;观察组男性54例、女性36例,年龄39~69岁、平均( $48.65 \pm 2.63$ )岁,病程1~5年、

平均( $3.81 \pm 0.85$ )年,治疗史1个月至3年、平均( $1.91 \pm 0.31$ )年。两组一般资料无明显差异( $P > 0.05$ )。

### 2.2 临床疗效

治疗后,观察组临床疗效评价有效率高于对照组,差异有统计学意义(96.67% vs. 66.67%,  $P < 0.001$ ),见表1。

### 2.3 疼痛情况

用药后两组VAS评分均下降,观察组显著低于对照组( $1.18 \pm 0.58$  vs.  $2.67 \pm 0.92$ ,  $P < 0.001$ ),见表2。

### 2.4 尿酸、血沉、C反应蛋白

治疗后两组UA、ESR及CRP均下降,观察组显著低于对照组( $P < 0.001$ ),见表3。

### 2.5 不良反应

治疗期间,观察组与对照组药物相关不良反应发生率比较,差异无统计学意义(23.33% vs. 18.89%,  $P=0.363$ ),见表4。

表1 两组临床疗效比较 ( $n, \%$ )

Table 1. Comparison of clinical efficacy between two groups ( $n, \%$ )

组别	显效	有效	无效	总有效率
对照组 ( $n=90$ )	30 (33.33)	30 (33.33)	30 (33.33)	60 (66.67)
观察组 ( $n=90$ )	59 (65.56)	28 (31.11)	3 (3.33)	87 (96.67)
$\chi^2$ 值				27.050
$P$ 值				<0.001

表2 两组治疗前后VAS评价分数比较 ( $\bar{x} \pm s$ )

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

组别	治疗前	治疗后
对照组 ( $n=90$ )	$6.23 \pm 1.42$	$2.67 \pm 0.92$
观察组 ( $n=90$ )	$6.41 \pm 1.15$	$1.18 \pm 0.58$
$t$ 值	0.935	12.997
$P$ 值	0.351	<0.001

表3 两组患者治疗前后尿酸、血沉、C反应蛋白比较 ( $\bar{x} \pm s$ )

Table 3. Comparison of UA, ESR and CRP between two groups before and after treatment ( $\bar{x} \pm s$ )

组别	UA (umol/L)		ESR (mm/h)		CRP (mg/L)	
	治疗前	治疗后	治疗前	治疗后	治疗前	治疗后
对照组 ( $n=90$ )	$641.29 \pm 37.86$	$342.89 \pm 31.52$	$33.56 \pm 6.24$	$22.56 \pm 7.40$	$21.31 \pm 6.02$	$13.71 \pm 4.58$
观察组 ( $n=90$ )	$649.73 \pm 41.05$	$301.27 \pm 32.19$	$35.03 \pm 7.45$	$18.12 \pm 6.17$	$20.98 \pm 5.89$	$7.21 \pm 2.52$
$t$ 值	1.434	8.764	1.252	9.352	0.372	11.796
$P$ 值	0.153	<0.001	0.536	<0.001	0.711	<0.001

表4 两组患者治疗期间药物相关不良反应比较 (n, %)

Table 4. Comparison of drug-related adverse reactions between two groups during treatment (n, %)

组别	肝功能异常	头痛	恶心呕吐	腹泻	发生率
对照组 (n=90)	5 (5.56)	5 (5.56)	5 (5.56)	2 (2.22)	17 (18.89)
观察组 (n=90)	7 (7.78)	5 (5.56)	7 (7.78)	2 (2.22)	21 (23.33)
$\chi^2$ 值					0.829
P值					0.363

### 3 讨论

生活质量的提升直接改变了人们的饮食与作息习惯,也导致多种疾病的发病率明显上升,痛风是其中对患者生活质量影响相对严重的一种<sup>[8]</sup>。痛风为嘌呤代谢异常全身性疾病,尿酸增高导致关节及其周围组织沉积尿酸盐结晶并产生急性炎症反应,典型临床表现为关节疼痛、红肿发热、活动受到明显限制,部分病情严重的可于肾脏出现结石<sup>[9-11]</sup>。对痛风患者的管理主要包括生活习惯调整及药物治疗,如低嘌呤饮食、维持体重在合理范围、戒烟酒、每天摄入足量水分。在药物治疗方面,常用药有秋水仙碱、糖皮质激素、非甾体类抗炎药,但临床实践发现秋水仙碱、糖皮质激素存在药物相关副作用,不仅增加患者痛苦且降低治疗依从性。依托考昔是常规非甾体类抗炎药,但关于单一使用该药能否有效缓解患者病情并达到长期控制效果,还需要进一步探究<sup>[12]</sup>。

本研究在依托考昔治疗基础上联合非布司他以探讨联合治疗的临床价值。依托考昔为选择性环氧酶-2(COX-2)抑制剂类非甾体抗炎药物,具有解热、镇痛及抗炎效果。前列腺素是引起炎症、疼痛、发热的常见因素<sup>[13]</sup>,而COX-2在前列腺素合成中发挥重要作用,依托考昔对COX-2合成有着特异性的抑制作用,且不会造成血小板凝集及胃黏膜损伤,能较好地改善GA患者的疼痛症状<sup>[14]</sup>。非布司他的主要成分是非布佐司他,该成分为黄嘌呤氧化酶抑制剂,可降低机体血清中的尿酸水平,且不会对嘌呤、嘧啶合成及代谢过程中所产生的其他酶产生抑制作用。高尿酸症需长期用药控制,非布司他具有较好的降尿酸作用,用药后短期内即可发挥作用且不会引发严重不良反应,相较传统别嘌醇药物有明显优势<sup>[15-16]</sup>。

本研究采用非布司他联合依托考昔片治疗的观察组患者,在一个疗程后病情控制有效率高于

对照组,说明联合用药有助于缓解GA患者的关节肿胀、疼痛以及提高活动能力。观察组的疼痛改善程度优于对照组,虽然疗程后两组均从平均中等疼痛降至低等疼痛,但观察组更明显。依托考昔片作为GA的基础治疗药物,能够在较短时间内解热止痛,但患者尿酸还保持在较高水平,因此病情仍存在反复波动的风险,联合非布司他能够减少尿酸合成,避免患者出现尿酸结晶沉积恶化的风险<sup>[17-18]</sup>。两药机制不同但可发挥协同作用,这与侯喆<sup>[19]</sup>、魏从兵等<sup>[20]</sup>的研究结果相近。

综上所述,在对痛风性关节炎患者进行生活习惯调整的基础上,应用非布司他联合依托考昔有助于改善临床疗效,但未来仍有待于更多大样本的高质量研究进一步探索验证。

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