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阿夫唑嗪联合盐酸莫西沙星治疗慢性前列腺炎的疗效及对血清 TNF-α、IL-1β、PSP、M-CSF 水平的影响 *

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摘要 目的：探讨阿夫唑嗪联合盐酸莫西沙星治疗慢性前列腺炎的疗效及对血清肿瘤坏死因子 -α (TNF-α)、白细胞介素 -1β (IL-1β)、胰石蛋白(PSP)、巨噬细胞集落刺激因子(M-CSF)水平的影响。**方法：**选择 2014 年 12 月 ~2016 年 12 月于我院就诊的 98 例慢性前列腺炎患者，按不同治疗方式分为对组与研究组，每组 49 例。对照组接受盐酸莫西沙星治疗，研究组基于对照组加以阿夫唑嗪治疗。观察并比较两组的临床疗效，治疗前后血清 TNF-α、IL-1β、PSP、M-CSF 水平、慢性前列腺炎症状指数评分(NIH-CPSI)的变化及不良反应的发生情况。**结果：**治疗后，研究组总有效率为 95.91%，显著高于对照组(77.55%，P<0.05)。两组治疗后血清 TNF-α、IL-1β、PSP、M-CSF 水平、NIH-CPSI 评分均较治疗前显著下降，且研究组上述指标均明显低于对照组(P<0.05)。两组不良反应的发生率比较差异无统计学意义(P>0.05)。**结论：**阿夫唑嗪联合盐酸莫西沙星治疗慢性前列腺炎的疗效优于单用盐酸莫西沙星，可能与其显著降低血清 TNF-α、IL-1β、PSP、M-CSF 水平有关。

关键词：慢性前列腺炎；阿夫唑嗪；盐酸莫西沙星；疗效；肿瘤坏死因子 -α；白细胞介素 -1β；胰石蛋白；巨噬细胞集落刺激因子
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Efficacy of Alfuzosin Combined with Moxifloxacin Hydrochloride in Treatment of Chronic Prostatitis and Effect on Serum TNF-α, IL-1β, PSP and M-CSF Levels*

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ABSTRACT Objective: To research the efficacy of alfuzosin combined with moxifloxacin hydrochloride in the treatment of chronic prostatitis and effect on the serum tumor necrosis factor-α(TNF-α), interleukin-1β(IL-1β), pancreatic stone protein (PSP), macrophage colony stimulating factor (M-CSF) levels. **Methods:** 98 cases of patients with chronic prostatitis admitted from December 2014 to December 2016 were selected and divided into the control and the research group according to different treatment methods. The control group was treated with moxifloxacin hydrochloride, and the research group was treated with alfuzosin based on the control group. The curative effect, changes of serum TNF-α, IL-1β, PSP, M-CSF levels, chronic prostate inflammatory index score (NIH-CPSI) before and after treatment and incidence of adverse reactions were compared between two groups. **Results:** After treatment, the total effective rate of research group was 95.91%, which was significantly higher than that of the control group (77.55%, P<0.05). The serum TNF-α, IL-1β, PSP, M-CSF levels and NIH-CPSI scores of two group were all significantly lower than those before treatment, which were obviously lower in the research group than those of the control group (P<0.05). There was no statistically significant difference in the incidence of adverse reactions between the two groups(P>0.05). **Conclusion:** Alfuzosin combined with moxifloxacin hydrochloride was more effective in the treatment of chronic prostatitis than moxifloxacin alone, which might be related to reduce the serum TNF-α, IL-1β, PSP, M-CSF levels.

Key words: Chronic prostatitis; Alfuzosin; Moxifloxacin hydrochloride; Curative effect; Tumor necrosis factor-α; Interleukin-1β; Glucoprotein Macrophage colony stimulating factor

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前言

慢性前列腺炎是一种常见泌尿科疾病,发病率较高,有非细菌性及细菌性之分。其中,非细菌性前列腺炎是由免疫反应异常、神经内分泌因素等所致,并以盆腔慢性疼痛及尿道刺激为主要表现,病原体感染是细菌性前列腺炎的主要诱因,伴尿急、尿痛、尿潴留等下尿路感染症状[1,2]。研究表明慢性前列腺炎发生发展与系列细胞因子有着紧密联系,以 TNF-α、IL-1β、PSP、M-CSF 等炎症因子表现较为明显,期能够增血管通透性,引起红肿、疼痛等病理改变,而其浓度改变可间接反映病情变化情况[3,4]。大量实验显示抗生素为慢性前列腺炎的首选药物,多口服氟喹诺酮类抗生素。盐酸莫西沙星是其新型抗菌药,其抗菌谱比较广泛且活性较强,同时半衰期长,生物利用度较高,但有研究显示仅少数患者伴明确的感染源,因此多需辅助其他药物治疗[5,6]。阿夫唑嗪属α- 受体阻滞剂,能够使膀胱及前列腺平滑肌松弛,缓解下尿路疼痛及症状,但国内鲜有二者联合用药的报道[7]。因此,本研究主要探讨了阿夫唑嗪联合盐酸莫西沙星治疗慢性前列腺炎的疗效及对血清 TNF-α、IL-1β、PSP、M-CSF 水平的影响。

1 资料与方法

1.1 一般资料

选择 2014 年 12 月 ~2016 年 12 月于我院就诊的 98 例慢性前列腺炎患者,入选标准:符合慢性前列腺炎相关诊断标准[8]:伴反射性疼痛或者炎性反应,前列腺初诊提示软硬不均或者腺体饱满或者质地较韧或者炎性结节、可伴局限性压痛、体积可出现变化,前列腺液镜检提示卵磷脂小体消失或者减少、白细胞在 10 个 /HP 以上,超声波检测提示声像图呈轻度异常;心肝肾等功能未见异常;无药物及酒精依赖史。排除尿道狭窄、精囊炎等并发症;活动性溃疡;急性前列腺炎;过敏性体质。对照组年龄 24~52 岁,平均(37.65± 4.11)岁;病程 5 个月 ~3 年,平均(1.68± 0.65)年;前列腺液白细胞介素 22~30 个 /HP,平均(25.43± 1.50)个 /HP。研究组年龄 24~52 岁,平均(37.12± 4.50)岁;病程 5 个月 ~3 年,平均(1.65± 0.61)年;前列腺液白细胞介素 23~31 个 /HP,平均(25.79± 1.55)个 /HP。两组一般临床资料比较差异均无统计学意义(P>0.05),具有互比性。

1.2 治疗方法

对照组接受盐酸莫西沙星治疗,口服 0.4g 盐酸莫西沙星(0.4 g/ 片,国药准字:J20030001,批号 140921,苏州东瑞制药有限公司),tid。研究组基于对照组联合阿夫唑嗪治疗,口服 10 mg 阿夫唑嗪(10 m/ 片,国药准字:J20140019,批号 140821,江西汇仁药业有限公司),qd。两组均持续治疗 1 个月,期间嘱患者忌烟酒,勿骑马、骑车,避免性生活不良。

1.3 观察指标

1.3.1 **慢性前列腺炎症状指数评分(NIH-CPSI)观察** 于治疗前后评估 NIH-CPSI,包含 0~6 分生活质量、0~6 分症状影响、0~10 分排尿情况、0~21 分疼痛不适 4 项,总分为 43 分,病程程度与评分呈正相关[9]。

1.3.2 **疗效观察** NIH-CPSI 评分下降超过 90%,临床体征及表现全部消失,前列腺液中白细胞计数持续 2 次在 10 个 /HP 以下即治愈;NIH-CPSI 评分下降在 60%~90%之间,前列腺液中白细胞计数降低在 50%~90%即显效;临床体征及表现显著减轻,NIH-CPSI 评分下降在 30%~60%之间,前列腺液中白细胞计数降低在 25%~50%即好转;临床体征及表现未见改变,NIH-CPSI 评分下降在 30%以下,前列腺液中白细胞计数降低在 25%以下即无效。治愈、显效及好转均视作总有效[10]。

1.3.3 **指标检测** 于治疗前及结束时采集患者 2 mL 晨起静脉血,常规处理后并于低温环境中保存待检。TNF-α、IL-1β、PSP、M-CSF 按酶联免疫法进行,试剂盒均来自江西安健生物技术有限公司。

1.4 统计学分析

选用 SPPS18.0 进行本研究的数据处理,计量资料以($\bar{x}\pm s$)表示,组间比较选用 t 检验进行,用[(例)%]表示计数资料,组间比较采用 x^2 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组临床疗效的比较

研究组的治疗总有效率为 95.91%,显著高于对照组(77.55%,P<0.05),见表 1。

表 1 两组临床疗效的比较[(例)%]

Table 1 Comparison of the clinical curative effect between two groups[(n)%]

Groups	Cure	Effective	Improve	Invalid	Total effective rate
Control group(n=49)	2(4.08)	19(38.78)	17(34.70)	11(22.44)	38(77.55)
Research group(n=49)	8(16.33)	30(61.22)	9(18.37)	2(4.08)	47(95.92)[a]

Note: Compared with the control group, [a]P<0.05.

2.2 两组治疗前后血清 TNF-α、IL-1β、PSP、M-CSF 水平的比较

治疗前,两组血清 TNF-α、IL-1β、PSP、M-CSF 水平比较差异无统计学意义 (P>0.05);治疗后,两组血清 TNF-α、IL-1β、PSP、M-CSF 水平均较治疗前显著下降,且研究组以上指标明显低于对照组(P<0.05),见表 2。

2.3 两组治疗前后 NIH-CPSI 评分比较

治疗前,两组 NIH-CPSI 评分比较差异无统计学意义(P>0.05);治疗后,两组 NIH-CPSI 评分均较治疗前显著下降,且研究组 NIH-CPSI 评分明显低于对照组(P<0.05),见表 3。

2.4 两组不良反应的发生情况比较

两组不良反应发生率比较差异无统计学意义 (P>0.05),见表 4。

3 讨论

表 2 两组治疗前后血清 TNF-α、IL-1β、PSP、M-CSF 水平的比较($\bar{x}\pm s$)

Table 2 Comparison of the serum TNF-α, IL-1β, PSP and M-CSF levels between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	Time	TNF-α(μg/L)	IL-1β(μg/L)	PSP(μg/L)	M-CSF(μg/L)
Control group(n=49)	Before treatment	1.98± 0.23	3.50± 0.43	38.90± 4.32	1.53± 0.19
	After treatment	1.16± 0.14[b]	1.34± 0.17[b]	16.57± 2.09[b]	0.51± 0.06[b]
Research group(n=49)	Before treatment	1.97± 0.22	3.52± 0.41	38.12± 4.10	1.52± 0.17
	After treatment	0.96± 0.11[ab]	0.95± 0.12[ab]	13.09± 1.62[ab]	0.44± 0.05[ab]

Note: Compared with the control group, [a]P<0.05; Compared with before treatment, [b]P<0.05.

表 3 两组治疗前后 NIH-CPSI 评分比较($\bar{x}\pm s$)

Table 3 Comparison of the NIH-CPSI score between two groups before and after the treatment ($\bar{x}\pm s$)

Groups	Time	Dysuria(points)	Pain(V)	Quality of life(points)	Symptoms(points)
Control group(n=49)	Before treatment	6.29± 0.78	15.20± 2.09	4.32± 0.54	6.59± 0.83
	After treatment	4.70± 0.56[b]	7.82± 0.96[b]	2.13± 0.25[b]	2.30± 0.27[b]
Research group(n=49)	Before treatment	6.34± 0.71	15.65± 2.27	4.41± 0.57	6.64± 0.87
	After treatment	3.15± 0.37[ab]	4.61± 0.61[ab]	1.30± 0.17[ab]	1.01± 0.12[ab]

Note: Compared with the control group, [a]P<0.05; Compared with before treatment, [b]P<0.05.

表 4 两组不良反应的发生情况比较[例(%)]

Table 4 Comparison of the incidence of adverse reactions between two groups[n (%)]

Groups	Gastrointestinal discomfort	Headache	Weak	Adverse reaction rate
Control group(n=49)	3(6.12)	2(4.08)	4(8.16)	9(18.37)
Research group(n=49)	2(4.08)	2(4.08)	3(6.12)	7(14.29)

慢性前列腺炎是男性生殖系统的多发性疾病，且可反复发作，难以根治，容易引起慢性精囊炎、阳萎、附睾炎、不育症等并发症[11]。尽可能的缓解患者排尿症状，改善疼痛并提高生活质量是其治疗目标。慢性前列腺炎多是因尿路逆行感染所致，多个临床研究显示此类患者前列腺按摩液中含有滴虫、淋球菌、支原体、粪球菌、大肠杆菌等病原菌[12]。因此，抗菌治疗是慢性前列腺炎的重要手段。氟喹诺酮类抗生素属化学合成抗菌药，由于抗菌谱广泛且活性强、生物后效应较明显，经口服吸收后的利用度高，且半衰期长，为抗菌的首选药物，既往多应用于腹腔、骨关节、尿路、呼吸道以及皮肤软组织、肠道、等感染治疗[13]。莫西沙星是氟喹诺酮类药物的第 4 代药物，其化学结构不同于其他氟喹诺酮类药物，由于增加了甲氧基团，可明显提高药物结合细菌的能力及对细胞膜的破坏力，其抗菌后效应可更持久[14]。同时，莫西沙星对抗厌氧菌及革兰阳性菌的活性更强，可提高对青霉素等耐药菌的效果，其经静脉或者口服给药后起效迅速，且穿透力强，可广泛分布于组织中，使细菌相关酶受到抑制，影响 DNA 复制，诱导病原菌凋亡、坏死[15]。但动物研究显示慢性前列腺炎患者应用盐酸莫西沙星治疗的疗效并不理想，考虑与前列腺炎的解剖位置较为特殊，且前列腺屏障能够降低药物渗透性，抑制炎性代谢物的分泌有关[16]。有研究显示抗生素的不正确使用不仅能够降低疗效，且可引起肝肾受损及菌群失调等副反应，本研究结果也显示单用盐酸莫西沙星组总有效率相对较低，提示其存在一定的局限性[17]。

阿夫唑嗪能够结合 α 肾上腺受体，抑制相应药物及神经递质结合 α 受体，发挥抗肾上腺素目的，其起效较为缓慢，但作用较为持久，药效强[18]。有研究报道，盐酸莫西沙星联合阿夫唑嗪治疗的有效率较高，仅少数患者作用较不明显[19]，本研究也显示二者联合治疗组临床疗效明显优于单用盐酸莫西沙星组，提示其临床效果确切，可能与二者作用机制不同，从而起到协同作用，提高疗效。

慢性前列腺炎发病机制未明，病因学十分复杂，存在广泛争议，可能是由多种细胞因子介导的炎症反应。TNF-α 是一种典型促炎性因子，可刺激其他细胞因子的生成。机体发生外源性感染时，由于抵抗能力较弱，能够诱导机体分泌过度 TNF-α，并可激活免疫应答反应，形成大量的免疫复合物，诱导单核细胞大量释放 TNF-α[20]。IL-1β 主要于细菌及内毒素刺激下由巨噬细胞与单核细胞分泌，能够协同刺激 APC 和 T 细胞活化，促进 B 细胞增殖和分泌抗体，调节机体的细胞免疫，浓度较高时能够引起内分泌效应，诱导肝脏急性期的蛋白合成，且可导致发热和恶病质，加剧机体损伤[21]。PSP 是一种急性时相蛋白，能够客观反应机体炎症状态，炎症反应期间纤维原细胞、内皮细胞能够刺激 PSP 生成，同时 PSP 又进一步激活淋巴细胞及中性粒细胞，启动免疫系统，产生恶性循环[22]。M-CSF 是炎症反应的特异标志物，来自于受损内皮细胞，能够刺激单核细胞分化、生长，能够于机体免疫反应中发挥关键作用[23,24]。

本研究结果显示两组治疗前 TNF-α、IL-1β、PSP、M-CSF 均明显上升，证实慢性前列腺炎是多种细胞因子共同作用所致，且经治疗后血清 TNF-α、IL-1β、PSP、M-CSF 均有一定降

低,但阿夫唑嗪联合盐酸莫西沙星组下降更明显,说明二者联合治疗能够纠正机体炎症反应,调整机体内环境,从而为疾病恢复创造良好的条件。同时,本研究结果显示阿夫咪唑联合盐酸莫西沙星组 NIH-CPSI 评分明显低于单用盐酸莫西沙星组,进一步证实其可行性高,能减轻患者临床症状。两组用药期间均有少数不良反应发生,但症状均比较轻微,未对进一步治疗产生影响。但本研究由于纳入样本量不足,观察时间较短,结果可能存在一定的偏差,建议增加样本量,延长观察时间。

综上所述,阿夫唑嗪联合盐酸莫西沙星治疗慢性前列腺炎的疗效优于单用盐酸莫西沙星, 可能与其显著降低血清 TNF-α、IL-1β、PSP、M-CSF 水平有关。

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