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普适泰治疗慢性 IIIA 型前列腺炎患者的疗效及对前列腺液 IFN- γ 、TGF- β_1 的影响 *

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摘要 目的:探讨普适泰治疗慢性 IIIA 型前列腺炎患者的疗效及对前列腺液干扰素- γ (IFN- γ)、转化生长因子- β_1 (TGF- β_1)的影响。**方法:**选择 2018 年 1 月至 2019 年 6 月我院接诊的 120 例慢性 IIIA 型前列腺炎患者,通过随机数表法分为观察组和对照组,每组 60 例。在常规处理基础上,对照组给予左氧氟沙星、坦索罗辛缓释胶囊治疗,观察组在对照组基础上,联合普适泰片治疗,均连续治疗连续用药 12 周。比较两组临床疗效、美国国立卫生研究院慢性前列腺炎症状指数(NIH-CPSI)、前列腺液白细胞计数(WBC)、卵磷脂小体(HP)、IFN- γ 、TGF- β_1 的变化及不良反应。**结果:**治疗后,观察组临床疗效总有效率为 93.33%,明显高于对照组的 78.33%,差异有统计学意义($P < 0.05$);观察组 NIH-CPSI 评分中疼痛和不适、排尿症状、症状严重程度及总分均明显低于对照组[(5.05±0.69)vs(6.33±0.74)分, (1.56±0.43)vs(2.70±0.55)分, (6.31±1.50)vs(7.92±1.64)分, (12.92±2.44)vs(16.95±2.87)分],差异有统计学意义($P < 0.05$);观察组前列腺液 WBC、IFN- γ 、TGF- β_1 明显低于对照组[(8.52±1.70)vs(10.04±1.58)个/HP, (8.06±1.32)vs(9.72±1.61)ng/L, (27.34±3.06)vs(42.57±3.89)ng/L],HP 明显比对照组高[(81.06±5.75)vs(70.22±6.31)%],差异有统计学意义($P < 0.05$);两组治疗期间恶心呕吐、乏力、心悸的总发生率比较差异无统计学意义($P > 0.05$)。**结论:**在常规治疗基础上,联合普适泰治疗慢性 IIIA 型前列腺炎患者疗效显著,可有效促进症状恢复,降低前列腺液 IFN- γ 、TGF- β_1 的表达,且不增加不良反应,值得应用推广。

关键词:慢性 IIIA 前列腺炎;普适泰;前列腺液;干扰素- γ ;转化生长因子- β_1

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The Effect of Prostat in the Treatment of Chronic IIIA Prostatitis and Its Effects on Prostatic Fluid IFN- γ and TGF- β_1 Levels*

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ABSTRACT Objective: To study the effect of prostat in the treatment of chronic IIIA prostatitis and its effects on prostatic fluid interferon- γ (IFN- γ) and transforming growth factor- β_1 (TGF- β_1) levels. **Methods:** 120 patients of chronic IIIA prostatitis who received therapy from January 2018 to June 2019 in our hospital were selected, according to the random number table, they were divided into the observation group and the control group, each group had 60 cases. On the basis of routine treatment, the control group was treated with levofloxacin and tamsulosin sustained-release capsule, and the observation group was combined with prostat tablet on the basis of the control group, they were treated continuously for 12 weeks. The clinical efficacy, the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), prostatic fluid white blood cell count (WBC), lecithin corpuscle (HP), IFN- γ and TGF- β_1 and adverse reactions were compared between the two groups. **Results:** After treatment, the total effective rate in the observation group was 93.33%, which was significantly higher than those in the control group 78.33%, the difference has statistically significant($P < 0.05$); the NIH-CPSI scores of pain and discomfort, urination symptoms, symptom severity and total scores in the observation group were significantly lower than those in the control group[(5.05±0.69) vs (6.33±0.74)scores, (1.56±0.43) vs (2.70±0.55)scores, (6.31±1.50) vs (7.92±1.64)scores, (12.92±2.44) vs (16.95±2.87)scores], the difference has statistically significant($P < 0.05$); the prostatic fluid WBC, IFN- γ and TGF- β_1 in in the observation group were significantly lower than those in the control group[(8.52±1.70) vs (10.04±1.58)number/HP, (8.06±1.32) vs (9.72±1.61)ng/L, (27.34±3.06) vs (42.57±3.89)ng/L], the HP were significantly lower than those in the control group [(81.06±5.75) vs (70.22±6.31)%], the difference has statistically significant ($P < 0.05$); there was no significant difference in the total incidence of nausea and vomiting, fatigue and palpitation between the two groups ($P > 0.05$). **Conclusion:** On the basis of conventional treatment, the treatment of chronic IIIA prostatitis with combination of propranolol has a significant effect, which can effectively promote the recovery

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of symptoms, reduce the expression of prostatic fluid IFN- γ and TGF- β_1 , and do not increase the adverse reactions, it's worth popularizing.

Key words: Chronic IIIA prostatitis; Prostat; Prostatic fluid; Interferon- γ ; Transforming growth factor- β_1

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前言

前列腺炎是临床上常见的男性泌尿系统疾病,国外的前列腺发病率约为 9%,而我国的发病率约为 8.5%,占泌尿男科门诊患者中的 1/3^[1,2]。IIIA 前列腺炎是其中最为常见的类型,发病后患者可出现排尿异常、骨盆部位慢性疼痛等症状,对患者的生活质量有着严重影响^[3,4]。临床上治疗慢性 IIIA 型前列腺炎的方案主要包括经验性口服氟喹诺酮类抗生素、 α 受体阻滞剂、M 受体阻滞剂等,但总体疗效仍有可提示的空间^[5,6]。植物制剂是目前较多学者的研究热点,有研究指出,植物类制剂普遍具有抗炎、抗雄激素样等药理效果,在治疗慢性 IIIA 型前列腺炎上也可取得一定成效^[7]。

慢性 IIIA 型前列腺炎的发病机制中涉及到多因素的综合作用,包括盆底神经肌肉异常、机体炎症、免疫功能紊乱等,近年来有较多报道也发现,干扰素- γ (IFN- γ)、转化生长因子- β_1 (TGF- β_1) 所产生的一系列免疫炎症反应在其中发挥着重要作用^[8,9]。因此,本研究在常规治疗上,联合植物类制剂普适泰治疗慢性 IIIA 型前列腺炎患者,旨在探讨其疗效及对前列腺液 IFN- γ 、TGF- β_1 的影响,现报道如下。

1 资料与方法

1.1 一般资料

选择 2018 年 1 月至 2019 年 6 月我院接诊的 120 例慢性 IIIA 型前列腺炎患者纳入研究,纳入标准:①符合慢性 IIIA 型诊断标准^[10],出现尿频、尿急、尿痛以及盆腔区域不适、疼痛等症状,通过前列腺液或者前列腺按摩液(EPS)检查,白细胞计数(WBC) ≥ 10 个/HP,卵磷脂小体(HP) $\leq$ +++/HP,细菌培养结果为阴性,并通过 B 超、前列腺指检等辅助检查确诊;②美国国立卫生研究院慢性前列腺炎症状指数(NIH-CPSI)^[11] ≥ 10 分;③病程 ≥ 3 个月;④签署研究知情同意书。排除标准:①急性前列腺炎或其余类型前列腺炎;②有前列腺炎、尿路感染史;③既往接受过前列腺手术、盆腔手术等泌尿系手术;④由于性传播疾病、睾丸附睾疾病、精索疾病、腰椎间盘突出所致的骨盆区域疼痛;⑤合并其余泌尿系统疾病或并发前列腺增生;⑥近 1 个月内服用过抗生素、非甾体类抗炎药、 α 受体阻滞剂、植物制剂等;⑦合并其余躯体重大疾病、恶性肿瘤、精神障碍等;⑧对研究药物有使用禁忌症。通过随机数表法分为观察组和对照组,每组 60 例,观察组年龄 23~51 岁,平均(39.83 $\pm$ 8.40)岁,对照组 22~48 岁,平均(39.29 $\pm$ 9.12)岁,观察组病程 5~15 个月,平均(9.87 $\pm$ 2.49)月,对照组 4~16 个月,平均(9.97 $\pm$ 2.27)月,差异无统计学意义($P > 0.05$)。

1.2 方法

两组治疗期间均给予常规处理,包括叮嘱患者加强体育锻炼、性生活不宜频繁、忌食辛辣刺激食物和烟酒等。对照组在此

基础上,给予左氧氟沙星(规格 0.1 g,厂家:北京第一三共制药有限公司,国药准字 H20000655)口服,0.1 g/次,2 次/d,连续用药 4 周,并予以坦索罗辛缓释胶囊(规格 0.2 mg,厂家:中国安斯泰来制药有限公司,国药准字 H20000681),0.2 mg/次,1 次/d,连续用药 12 周。观察组在对照组基础上,联合普适泰片(规格:每片含花粉提取物 P5 70 mg 和花粉提取物 EA10 4 mg,厂家:南京美瑞制药有限公司,国药准字 H20000486)治疗,1 片/次,2 次/d。连续用药 12 周。

1.3 观察指标

1.3.1 临床疗效 于治疗 12 周后,根据文献^[12]评价,临床控制:排尿正常,前列腺及盆腔区域无疼痛感,NIH-CPSI 评分得到 $\geq 95\%$ 的减少,不同日连续 2 次或以上 EPS 检查结果正常;显效:和治疗前相比,排尿情况、前列腺及盆腔疼痛均明显改善,NIH-CPSI 评分减少 60%~94%,EPS 检查 WBC 降低 $\geq 60\%$;有效:排尿情况、前列腺及盆腔疼痛部分缓解,NIH-CPSI 评分减少 30%~59%,EPS 检查 WBC 降低 30%~59%;无效:和治疗前相比症状、NIH-CPSI 评分和 EPS 检查均无明显改善。总有效率 = 临床控制率 + 显效率 + 有效率。

1.3.2 NIH-CPSI 评分 记录治疗前、治疗后 12 周后的变化,该评分内容包括疼痛和不适评分、排尿症状评分、症状严重程度评分及总分 4 个部分,总分 1~14 分为轻度,15~29 分为中度,30~43 分为重度;

1.3.3 EPS 检查 于治疗前、治疗后 12 周后接受 EPS 检查,方法如下:排尿后使用碘伏对阴茎头、尿道外口进行消毒,患者处于胸膝体位,接受肛门指检后进行前列腺按摩,收集 2 mL 前列腺液,取 1 滴进行常规镜检,记录 WBC、HP 的表达;另外前列腺液储存 Eppendorf 管中,并于 -70℃ 的液氮保存,使用北京晶美公司生产的酶联免疫吸附法(ELISA)试剂盒检测 IFN- γ 、TGF- β_1 的表达,仪器选用奥地利 BIO CELL 全自动酶标仪;

1.3.4 记录治疗期间不良反应

1.4 统计学分析

以 spss18.0 软件包处理数据,计量资料用均数 $\pm$ 标准差($\bar{x} \pm s$)表示,采用 t 检验,计数资料组间比较采用 χ^2 检验,以 $P < 0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组临床疗效比较

观察组临床疗效总有效率为 93.33%,明显高于对照组的 78.33%($P < 0.05$),见表 1。

2.2 两组 NIH-CPSI 评分比较

治疗后,两组 NIH-CPSI 评分中疼痛和不适、排尿症状、症状严重程度及总分较治疗前均明显降低($P < 0.05$),观察组 NIH-CPSI 评分中疼痛和不适、排尿症状、症状严重程度及总分均明显低于对照组($P < 0.05$),见表 2。

表 1 两组临床疗效比较[n(%)]

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

Groups	Clinical control	Markedly effective	Valid	Invalid	Total effective rate
Observation group(n=60)	15(25.00)	30(50.00)	11(18.33)	4(6.67)	56(93.33)*
Control group(n=60)	9(15.00)	20(33.33)	18(30.00)	13(21.67)	47(78.33)

表 2 两组 NIH-CPSI 评分比较($\bar{x} \pm s$, 分)Table 2 Comparison of the NIH-CPSI scores between two groups($\bar{x} \pm s$, scores)

Groups		Pain and discomfort	Urination symptoms	Symptom severity	Total score
Observation group (n=60)	Before treatment	10.73±2.45	5.63±0.86	12.18±2.48	28.54±3.21
	After treatment	5.05±0.69* [#]	1.56±0.43* [#]	6.31±1.50* [#]	12.92±2.44* [#]
Control group(n=60)	Before treatment	10.50±2.90	5.71±0.82	12.09±2.82	28.30±3.58
	After treatment	6.33±0.74*	2.70±0.55*	7.92±1.64*	16.95±2.87*

Note: Vs the before treatment, * $P < 0.05$; vs the control group, [#] $P < 0.05$.

2.3 两组前列腺液 WBC、HP 比较

($P < 0.05$), 观察组前列腺液 WBC 明显低于对照组, HP 明显比
治疗后, 两组前列腺液 WBC 均明显降低, HP 明显升高 对照组高($P < 0.05$), 见表 3。

表 3 两组前列腺液 WBC、HP 比较($\bar{x} \pm s$)Table 3 Comparison of the prostatic fluid WBC and HP between two groups($\bar{x} \pm s$)

Groups		WBC(number/HP)	HP(%)
Observation group(n=60)	Before treatment	15.17±2.69	41.54±4.63
	After treatment	8.52±1.70* [#]	81.06±5.75* [#]
Control group(n=60)	Before treatment	15.08±2.75	41.87±4.20
	After treatment	10.04±1.58*	70.22±6.31*

Note: Vs the before treatment, * $P < 0.05$; vs the control group, [#] $P < 0.05$.

2.4 两组前列腺液 IFN- γ 、TGF- β_1 比较

观察组前列腺液 IFN- γ 、TGF- β_1 明显低于对照组($P < 0.05$), 见
治疗后, 两组前列腺液 IFN- γ 、TGF- β_1 均明显降低($P < 0.05$), 表 4。

表 4 两组前列腺液 IFN- γ 、TGF- β_1 比较($\bar{x} \pm s$, ng/L)Table 4 Comparison of the prostatic fluid IFN- γ and TGF- β_1 between two groups($\bar{x} \pm s$, ng/L)

Groups		IFN- α	TGF- β_1
Observation group(n=60)	Before treatment	15.63±2.49	68.91±7.53
	After treatment	8.06±1.32* [#]	27.34±3.06* [#]
Control group(n=60)	Before treatment	15.61±2.77	69.20±7.22
	After treatment	9.72±1.61*	42.57±3.89*

Note: Vs the before treatment, * $P < 0.05$; vs the control group, [#] $P < 0.05$.

2.5 不良反应

意义($P > 0.05$), 见表 5。

两组恶心呕吐、乏力、心悸的总发生率比较差异无统计学

表 5 两组不良反应比较[n(%)]

Table Comparison of the adverse reaction between two groups[n(%)]

Groups	Nausea and vomiting	Fatigue	Palpitation	Total incidence rate
Observation group(n=60)	4(6.67)	1(1.67)	0(0.00)	5(8.33)
Control group(n=60)	2(3.33)	1(1.67)	1(1.67)	4(6.67)

3 讨论

慢性前列腺炎是临床上常见的男性疾病, 在中青年男性中

的发病率较高, 约为 30%~40%, 随着近年来经济发展、生活节奏的加快, 前列腺炎的发生也对患者的生活质量及身心健康带来了较多影响^[13, 14]。I 型和 II 型前列腺炎主要是由于病原

体感染所致,IIIA型前列腺炎在前列腺患者中约占90%以上,是最常见的前列腺类型,临床症状主要表现为尿急、尿痛、排尿异常、盆骨区域疼痛等,其病因大多数和过度疲劳、长期抽烟喝酒、运动量较少等相关,但在具体的发病机制方面较为复杂,涉及到多因素综合作用,这也增加了临床治疗前列腺炎的难度^[15,16]。

对于IIIA型前列腺炎患者的治疗目的是改善排尿症状、缓解疼痛等,以期提高患者生活质量,在药物治疗方案中,包括抗生素、 α 受体阻滞剂等。左氧氟沙星可通过对DNA合成产生干扰,杀死机体病原体,缓解机体病原体感染,促进症状改善^[17,18]。坦索罗辛是较为常用的一类 α 受体阻滞剂,可通过选择性的阻断前列腺中的 α_1 肾上腺素受体,对前列腺、膀胱等部位的平滑肌具有持续性的松弛作用,达到改善排尿疼痛、骨盆疼痛及下尿路症状的目的^[19,20]。但在临床实践中也发现,上述常规疗法的总体疗效仍不尽人意,且停药后仍有部分患者容易复发^[21,22]。植物类制剂也是目前治疗前列腺炎的研究热点,普适泰主要提取自纯种裸麦花粉,有效成分包括P5和EA10,其中P5为水溶性物质阿魏酰 γ -丁二胺,EA10为脂溶性物质生长素,具有抗炎、抗雄激素样效果^[23,24]。有基础实验显示,普适泰对非细菌性前列腺炎小鼠模型的前列腺血流具有改善作用,且可通过减少WBC的途径,发挥抑制小鼠机体炎症反应过度释放的效果,促进组织修复,且其对睾酮转变为二氢睾酮的途径具有抑制作用,可从多种作用机制改善非细菌性前列腺炎炎症状态^[25]。并有报道显示,普适泰有助于改善中重度老年前列腺增生患者前列腺组织炎症,减少相关并发症发生率^[26]。

本研究结果显示,联合普适泰治疗的患者临床疗效总有效率高达93.33%,明显比常规治疗患者的78.33%更高,且联合普适泰治疗的患者NIH-CPSI评分中各项指标的改善程度也明显优于常规治疗的患者,分析可能是由于在普适泰的有效成分中,P5和EA10对膀胱逼尿肌的收缩、尿道平滑肌松弛具有促进作用,可帮助尿道内压力的降低,改善前列腺内尿液反流情况,调节局部微缓解,加上常规治疗中左氧氟沙星的抗炎效果、坦索罗辛的改善排尿症状效果,联合用药方案,从多重作用发挥疗效,进一步促进患者排尿功能恢复,缓解前列腺炎症,提高疗效。

国内外均有研究指出,在前列腺炎的发生、发展过程中,某些细胞因子所介导的炎症反应发挥着重要作用,并逐渐收到了临床学者的重视^[27,28]。IFN- γ 是一种重要的促炎细胞因子,对T淋巴细胞、巨噬细胞等免疫细胞的增殖及活性均IFN- γ 具有促进作用。在前列腺炎患者中,由于病原体或其他致病因子的刺激下,会激活前列腺局部巨噬细胞,生成白细胞介素(IL)、肿瘤坏死因子(TNF)等促炎因子,而巨噬细胞作为抗原递呈细胞,又可激活T淋巴细胞,生成IFN- γ ,参与着机体炎症反应过程^[29,30]。TGF- β_1 是一类具有双重效应的多功能因子,在正常生理状况下,其对炎症、细胞增生等过程具有抑制作用,但其表达过量,可刺激组织内细胞分化成纤维细胞,并合成细胞外基质,加重炎症反应^[31,32]。Wang R等^[33]研究也指出,在前列腺炎患者血清和前列腺液中TGF- β_1 的表达出现明显升高,其可通过上调前列腺局部炎症因子的转录,促使炎症细胞浸润、聚集,加重患者炎症反应和疼痛程度。

本研究结果显示,联合普适泰治疗的患者前列腺炎中前列腺液IFN- γ 、TGF- β_1 的降低程度明显更高,且WBC、HP的改善程度也更明显,显示出联合普适泰可提高抗炎效果,有研究显示,在普适泰的有效成分中,脂溶性物质EA10中富含3 β -甾醇,可通过对环氧合酶、脂和酶的活性产生抑制作用,降低前列腺素、白三烯等内源性炎症物质的合成,并可缓解膀胱三角区充血、水肿等症状,促使局部炎症消退,发挥抑制炎症反应的效果^[34,35]。在本研究中的不良反应的观察中也显示,两组总发生率比较差异无统计学意义,显示出普适泰具有较好的安全性,联合用药也未增加不良反应。此外,在临床应用中也需注意,普适泰药效持续时间长、起效较慢,短期应用可能疗效不足,本研究患者持续应用了12周取得了较好的临床疗效,在今后的治疗中也需叮嘱患者需坚持用药。但本研究也存在着不足,例如前列腺炎是一种复发率较高的疾病,本研究由于时间限制,未持续随访停药后患者的复发情况,对于此部分内容此后仍需进一步深入探讨。

综上所述,在常规治疗基础上,联合普适泰治疗慢性IIIA型前列腺炎患者疗效显著,可有效促进症状恢复,降低前列腺液IFN- γ 、TGF- β_1 的表达,且不增加不良反应,值得推广应用。

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