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丹黄祛瘀胶囊联合阿奇霉素对慢性盆腔炎患者血液流变学和血清炎症因子的影响*

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摘要 目的:观察阿奇霉素联合丹黄祛瘀胶囊在慢性盆腔炎患者中的应用价值。**方法:**研究病例选自2019年6月至2021年6月期间我院收治的慢性盆腔炎患者127例,采用随机数字表法将符合要求的患者分为对照组(63例,阿奇霉素治疗)和观察组(64例,丹黄祛瘀胶囊联合阿奇霉素治疗),两组均治疗2周。对比两组疗效、临床症状消失时间、血液流变学和血清炎症因子变化情况,观察两组不良反应的发生情况,并作记录。**结果:**观察组临床总有效率高于对照组($P<0.05$)。观察组的腰骶胀痛、下腹疼痛、带下异常等症消失时间短于对照组($P<0.05$)。观察组治疗2周后的白介素-6(IL-6)、白介素-1 β (IL-1 β)、C反应蛋白(CRP)低于对照组($P<0.05$)。观察组治疗2周后的全血高切黏度、全血低切黏度、纤维蛋白原及红细胞沉降率低于对照组($P<0.05$)。两组患者的不良反应发生率组间对比无统计学差异($P>0.05$)。**结论:**慢性盆腔炎在阿奇霉素治疗基础上联合丹黄祛瘀胶囊,症状得到明显缓解,同时还可改善机体血液流变学和炎症因子水平,临床应用价值较好。

关键词:丹黄祛瘀胶囊;阿奇霉素;慢性盆腔炎;血液流变学;炎症因子

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Effects of Danhuang Quyu Capsule Combined with Azithromycin on Hemorheology and Serum Inflammatory Factors in Patients with Chronic Pelvic Inflammatory Disease*

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ABSTRACT Objective: To observe the application value of Azithromycin combined with Danhuang Quyu capsule in patients with chronic pelvic inflammatory disease. **Methods:** 127 patients with chronic pelvic inflammatory disease who were treated in our hospital from June 2019 to June 2021 were selected, they were randomly divided into control group (63 cases, azithromycin treatment) and observation group (64 cases, Danhuang Quyu capsule combined with azithromycin treatment), both groups were treated for 2 weeks. The curative effect, disappearance time of clinical symptoms, hemorheology and changes of serum inflammatory factors were compared between the two groups. The occurrence of adverse reactions in the two groups were observed and recorded. **Results:** The total effective rate of the observation group was higher than that of the control group ($P<0.05$). The disappearance time of lumbosacral pain, lower abdominal pain and abnormal band in the observation group were shorter than those in the control group ($P<0.05$). The levels of interleukin-6 (IL-6), interleukin-1 β (IL-1 β), C-reactive protein (CRP) in the observation group at 2 weeks after treatment were lower than those in the control group ($P<0.05$). The whole blood high shear viscosity, whole blood low shear viscosity, fibrinogen and erythrocyte sedimentation rate in the observation group at 2 weeks after treatment were lower than those in the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** On the basis of azithromycin treatment, combined with Danhuang Quyu capsule, the symptoms of chronic pelvic inflammatory disease can be significantly alleviated. At the same time, it can also improve the level of Hemorheology and inflammatory factors. It has good clinical application value.

Key words: Danhuang Quyu capsule; Azithromycin; Chronic pelvic inflammatory disease; Hemorheology; Inflammatory factor

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前言

慢性盆腔炎是育龄期女性的多发病之一,主要病理改变为血液流变学异常和盆腔炎性渗出,具有病程长、病情缠绵、复

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发病率高等特点^[1,2]。既往有数据资料显示^[3],我国慢性盆腔炎的发病率约为15%~25%,近年来发病率更是呈现着升高的趋势,严重影响着妇女的生活质量。现临床有关该病的治疗主要以抗感染治疗为主,阿奇霉素抗菌作用强,主要用于敏感细菌引起的感染性疾病,适用于各种细菌感染性疾病^[4],但多次、重复、大剂量应用抗感染治疗必然会导致患者自身的免疫力低下,疾病迁延不愈^[5]。女性所患疾病大多数与血瘀有关,下腹疼痛是慢性盆腔炎患者血瘀证存在的最主要证据。丹黄祛瘀胶囊是治疗慢性盆腔炎的常用药物,具有活血化瘀、软坚散结、镇痛的功效^[6]。本次研究探讨阿奇霉素联合丹黄祛瘀胶囊治疗慢性盆腔炎的临床应用价值,以期为临床治疗提供推广依据。

1 资料与方法

1.1 临床资料

表1 两组患者的具体临床资料($\bar{x} \pm s$)

Table 1 Specific clinical data of the two groups($\bar{x} \pm s$)

Groups	Age(year)	Course of disease(year)	Body mass index(kg/m ²)	Package diameter(cm)
Control group(n=63)	42.19± 4.53	4.14± 0.75	24.59± 2.31	4.22± 0.31
Observation group(n=64)	42.32± 5.06	4.19± 0.83	24.86± 2.74	4.29± 0.28
t	-0.152	-0.356	-0.600	-1.336
P	0.879	0.722	0.532	0.184

1.2 方法

两组患者入院后均行常规的妇科检查,包括三大常规、妇检、B超、生化全套等常规检查。对照组患者口服阿奇霉素(国药准字H20066359,规格:0.5 g,石药集团欧意药业有限公司)治疗,1.0 g/次,1次/d。观察组在阿奇霉素(治疗方案同对照组一致)的基础上加用丹黄祛瘀胶囊(生产批号:国药准字Z20026010,规格:每粒装0.4 g,吉林龙鑫药业有限公司)治疗,口服,3粒/次,3次/d。两组均治疗2周。

1.3 疗效判定指标^[8]

治疗2周后患者下腹压痛等临床症状及体征均消失,腹部彩超显示盆腔积液和炎性包块消失,各项血象恢复至正常水平则为治愈。治疗2周后患者下腹压痛等临床症状及体征较治疗前减轻,腹部彩超显示盆腔积液及盆腔炎性包块直径较治疗前减少,血象接近正常则为好转。未能达到上述标准者则为无效。总有效率=治愈率+好转率。

1.4 观察指标

(1)观察并记录两组患者下腹疼痛、腰骶胀痛、带下异常消失时间。(2)治疗前、治疗2周后,在空腹状态下采集血样6 mL

研究病例选自2019年6月至2021年6月期间收治的127例慢性盆腔炎患者,患者临床主诉为下腹压痛,主要为附件区,盆腔可扪及炎性包块,诊断标准参考《妇产科学》^[7]进行。纳入标准:(1)有性生活史;(2)患者了解研究内容,签署知情同意书;(3)患者对本次研究的使用药物无禁忌。排除标准:(1)合并造血系统、免疫系统疾病的患者;(2)合并盆腔恶性肿瘤、盆腔癌性包块、异位妊娠等;(3)合并有严重急性感染等并发症;(4)合并肝肾功能障碍者;(5)哺乳期、妊娠期女性;(6)存在痴呆、精神障碍、认知功能障碍者。采用随机数字表法将符合要求的患者分为对照组(63例,阿奇霉素治疗)和观察组(64例,丹黄祛瘀胶囊联合阿奇霉素治疗),两组患者的具体临床资料列表如1,组间对比未见统计学差异($P>0.05$)。我院伦理委员会已批准本研究。

左右,经离心转速为3000 r/min,离心时间为15 min,离心半径为13 cm的条件下行离心处理,分离上清液后置于低温(-30℃)冰箱中待检测。采用北京赛科希德发展有限公司生产的SA6000自动血液流变仪检测全血高切黏度、全血低切黏度、纤维蛋白原及红细胞沉降率。采用酶联免疫吸附法检测血清白介素-6(IL-6)、白介素-1β(IL-1β)、C反应蛋白(CRP)水平,严格参考试剂盒(欧蒙医学诊断(中国)有限公司)说明书的参考步骤进行检测。(3)治疗期间观察两组用药安全性。

1.5 统计学方法

全部数据采用SPSS 21.0统计分析。用率(%)描述疗效、不良反应等计数资料,采用卡方检验,以均值±标准差的形式表示血液流变学、炎症因子等计量资料,组间比较行成组t检验,组内前后比较行配对t检验。检验水准 $\alpha=0.05$ 。

2 结果

2.1 治疗2周后疗效情况

对照组、观察组的临床总有效率为71.43%(45/63)、90.63%(58/64),组间对比差异有统计学意义($P<0.05$),见表2。

表2 治疗2周后疗效情况[例(%)]

Table 2 Efficacy after two weeks of treatment [n(%)]

Groups	Cure	Better	Invalid	Total effective rate
Control group(n=63)	16(25.40)	29(46.03)	18(28.57)	45(71.43)
Observation group(n=64)	22(34.38)	36(56.25)	6(9.38)	58(90.63)
χ^2				7.663
P				0.006

2.2 临床症状消失时间记录情况

与对照组相比,观察组的下腹疼痛、腰骶胀痛、带下异常等

症状消失时间明显缩短,组间对比差异有统计学意义($P<0.05$),见表3。

表3 临床症状消失时间记录情况($\bar{x}\pm s$,d)
Table 3 Record of disappearance time of clinical symptoms($\bar{x}\pm s$, d)

Groups	Lower abdominal pain	Lumbosacral pain	Subzonal anomaly
Control group(n=63)	12.13± 1.92	10.09± 1.71	8.41± 1.26
Observation group(n=64)	8.38± 1.71	7.16± 1.53	5.76± 1.19
t	11.628	10.180	12.187
P	0.000	0.000	0.000

2.3 两组不同观察时间点下的炎症因子变化情况

两组治疗前的IL-6、IL-1 β 、CRP对比无显著性差异($P>0.05$)。

05)。两组治疗2周后的IL-6、IL-1 β 、CRP较治疗前下降,且观察组低于对照组($P<0.05$),详见表4。

表4 两组不同观察时间点下的炎症因子变化情况($\bar{x}\pm s$)
Table 4 Changes of inflammatory factors in the two groups at different observation time points($\bar{x}\pm s$)

Groups	IL-6(pg/mL)		IL-1 β (pg/mL)		CRP(mg/L)	
	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment
Control group(n=63)	155.21± 29.87	97.63± 24.76*	30.67± 4.23	23.06± 5.31*	23.25± 6.74	14.38± 7.62*
Observation group(n=64)	154.73± 23.94	63.91± 18.19*	30.16± 5.38	14.53± 3.27*	22.89± 7.61	10.62± 6.49*
t	0.100	8.756	0.593	10.919	0.282	2.995
P	0.921	0.000	0.554	0.000	0.778	0.003

Note: * indicates that compared with before treatment, $P<0.05$.

2.4 两组不同观察时间点下的血液流变学指标变化情况

两组治疗前的全血高切黏度、全血低切黏度、纤维蛋白原及红细胞沉降率及红细胞沉降率对比无显著性差异($P>0.05$)。两组治疗2周后

的全血高切黏度、全血低切黏度、纤维蛋白原及红细胞沉降率较治疗前下降,且观察组低于对照组($P<0.05$),详见表5。

表5 两组不同观察时间点下的血液流变学指标变化情况($\bar{x}\pm s$)
Table 5 Changes of hemorheological indexes in the two groups at different observation time points($\bar{x}\pm s$)

Groups	Whole blood high shear viscosity(mPa·s)		Whole blood low shear viscosity(mPa·s)		Fibrinogen(g/L)		Erythrocyte sedimentation rate(mm/h)	
	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment	Before treatment	2 weeks after treatment
Control group(n=63)	4.28± 0.49	3.75± 0.46*	12.11± 1.52	8.99± 1.46*	5.61± 0.57	4.06± 0.63*	26.94± 4.57	17.04± 2.38*
Observation group(n=64)	4.34± 0.35	3.24± 0.35*	12.37± 1.42	6.35± 1.31*	5.66± 0.42	2.95± 0.41*	26.85± 4.78	12.81± 1.35*
t	-0.795	7.038	-0.996	10.729	-0.563	11.700	0.108	12.344
P	0.428	0.000	0.321	0.000	0.474	0.000	0.974	0.000

Note: * indicates that compared with before treatment, $P<0.05$.

2.5 两组患者不良反应发生情况

对照组治疗期间有2例出现腹泻、3例出现上腹部不适、1例出现恶心,不良反应发生率为9.52%。而观察组治疗期间有3例出现腹泻、3例出现上腹部不适、2例出现恶心,不良反应发

生率为12.50%。两组对比无差异($\chi^2=0.287, P=0.592$)。

3 讨论

慢性盆腔炎是指女性盆腔腹膜、内生殖器及其周围的结缔

组织受到细菌感染所致的炎性病变,可导致盆腔纤维组织粘连及增生、输卵管阻塞,最终引起盆腔肿块、慢性盆腔痛、不孕等后遗症^[9,10]。慢性盆腔炎患者的病原体来源有二:一为内源性病原体,以需氧菌和厌氧菌混合感染较为多见^[11];二为外源性病原体,主要为性传播的病原体^[12]。我国多数慢性盆腔炎患者感染是外源性病原体所致,患者受到外源性病原体侵入后,一可导致感染,二可刺激机体的免疫系统,而免疫系统的激活,可导致多种细胞因子大量释放,巨噬细胞被吸引、聚集、激活,引起局部炎症反应甚至全身反应^[13]。炎症可以致瘀引起血液流变学异常,进而引起血液循环和微循环障碍^[14]。因此,临床认为慢性盆腔炎患者血液流变性的改变,会导致其盆腔代谢和功能的失调,需引起临床的诊疗重视。阿奇霉素是一种大环内酯类抗生素,抗菌谱广泛,能够抑制多种革兰阳性球菌、支原体、衣原体、嗜肺军团菌^[15]。不少研究证实阿奇霉素用于慢性盆腔炎可获得一定的疗效^[16,17]。但从这些研究中也可看出,长期单一使用抗生素不能达到有效抑菌浓度,导致治疗效果欠佳,故常常选择联合用药^[18]。丹黄祛瘀胶囊是一种中成药,主要成分为败酱草、丹参、茯苓、土鳖虫、莪术、苦参、川楝子、当归、黄芪、鸡血藤、三棱、延胡索等^[19,20]。孟芳等^[21]学者认为,丹黄祛瘀胶囊可显著减轻慢性盆腔炎患者的炎性包块,疗效确切。吕伯中等人^[22]的研究结果也表明,丹黄祛瘀胶囊能够提高宫颈的抵御能力,改善其治疗效果。

本次研究结果中,阿奇霉素联合丹黄祛瘀胶囊可促进慢性盆腔炎患者症状改善,安全有效。阿奇霉素的主要抗菌机制在于能够结合敏感微生物 50 s 核糖体的亚单位,从而阻止敏感菌蛋白质的合成,发挥强效杀菌作用^[23]。而丹黄祛瘀胶囊方中败酱草、苦参、黄芪均有广谱抗菌作用^[24]。同时药理研究还证实丹黄祛瘀胶囊具有较好的抗炎作用,可通过修复患者因炎症而破损的组织,改善患者盆腔组织局部张力,发挥良好的辅助疗效^[25]。慢性盆腔炎的发生、发展均贯穿者炎症反应,IL-1 β 是一种前促炎因子,可促进 B 细胞和 T 淋巴细胞活化,并介导多种炎症因子的分泌^[26]。IL-6 能直接参与炎症反应,刺激肝细胞产生急性时相反应蛋白^[27]。CRP 是在机体受到感染或者组织损伤时,血清中急剧上升的蛋白质^[28]。本次研究结果提示,丹黄祛瘀胶囊联合阿奇霉素可有效控制慢性盆腔炎患者的炎症反应。药理研究结果显示^[29,30],茯苓具有抗炎及镇痛的作用;当归具有增强机体免疫力、抗炎、抗血小板聚集等作用;败酱草可增强网状细胞和白细胞的吞噬能力,从而达到抗菌消炎的作用。相关研究表明^[31,32],炎症与血瘀证在病理、病机及治疗方面存在密切的关系,炎症反应的长期激活可导致中性粒细胞和血管内皮细胞等氧自由基的生成和释放,而氧自由基可对人体产生病理性的损伤,可引起小血管和毛细血管收缩与闭塞,导致血液高凝。全血高切黏度、全血低切黏度、纤维蛋白原及红细胞沉降率均是临床常见的血液流变学指标,当其水平上升时,血液呈现高凝状态,一定程度上可加重慢性盆腔炎的疾病进展。本次研究显示,联合治疗的慢性盆腔炎患者其血液流变学改善效果更好,可能与丹黄祛瘀胶囊有效的控制机体炎症反应,从而改善血液流变学有关。

综上所述,丹黄祛瘀胶囊联合阿奇霉素可促进慢性盆腔炎患者症状改善,安全有效,同时在改善炎症因子水平、血液流变

学方面效果显著。

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