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双氯芬酸钠与塞来昔布治疗类风湿关节炎的疗效及对心血管的影响研究

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摘要 目的:探讨双氯芬酸钠和塞来昔布治疗类风湿关节炎的临床疗效及用药安全性。**方法:**将我院 2011 年 1 月 -2012 年 1 月门诊收治的 98 例类风湿性关节炎患者随机分为对照组和观察组,每组 49 例。对照组给予双氯芬酸钠治疗,观察组给予塞来昔布治疗,观察两组临床治疗效果及心血管不良事件的发生情况。**结果:**观察组总有效率为 91.84%显著高于对照组的 75.51%,两组比较差异具有统计学意义(P<0.05);观察组 ESR 及 CRP 分别为(110.65± 7.28)mm/h 和(10.42± 0.98)mg/L 显著低于治疗前和对照组,比较差异具有统计学意义(P<0.05);观察组心血管不良事件发生率为 8.16%显著低于对照组的 20.41%,两组比较差异具有统计学意义(P<0.05)。**结论:**塞来昔布治疗类风湿关节炎具有较好的临床疗效,可有效改善患者疼痛、僵硬或功能受限等症状,且心血管不良事件发生率低,值得临床进一步推广和应用。

关键词:双氯芬酸钠;塞来昔布;类风湿关节炎

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The Clinical Effect of Diclofenac and Celecoxib in Treatment of Rheumatoid Arthritis and its Effect on the Cardiovascular

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ABSTRACT Objective: To investigate the clinical efficacy and medication safety of diclofenac and celecoxib in the treatment of rheumatoid arthritis. **Methods:** 98 patients with the rheumatoid who were treated in our hospital from January 2011 to 2012 were selected and randomly divided into the control group and the observation group with 49 cases in each one. The patients in the control group were treated by the diclofenac, while the patients in the observation group were treated by the celecoxib. Then the clinical effect and the occurrence of adverse cardiovascular were observed and compared between two groups two groups. **Results:** In the observation group, the total effective rate in the observation group was 91.84%, the ESR was (110.65± 7.28) mm/h and the CRP was (10.42± 0.98) mg/L which were significantly different when comparing with the control group(P<0.05); the incidence of adverse cardiovascular events of patients in the observation group was 8.16% which was significantly lower than 20.41% in the control group (P<0.05). **Conclusion:** It is indicated that the effects of Celecoxib on the treatment of rheumatoid arthritis should be worthy to be promoted to the clinical with the advantages of better efficacy, and low incidence of adverse cardiovascular reactions.

Key words: Diclofenac; Celecoxib; Rheumatoid Arthritis

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前言

类风湿关节炎(rheumatoidarthritis,RA)是一种慢性多系统性炎症性的自身免疫疾病[1,2],临床主要表现为进行性、对称性、破坏性的关节及其周围组织的非感染性炎症反应,其中以手、腕、肘、膝、足和踝部等关节受累为主,病情反复迁延易导致患者关节畸形或功能障碍,具有较高的致残率和死亡率[3-5]。传统的非甾体抗炎药物(NSAIDs)是临床上治疗 RA 的主要药物,具有较好的临床治疗效果,但患者长期用药易出现胃肠道等不良反应,毒副作用较大,患者耐受性差,多数难以坚持治疗[6-8]。本研究选取我院 2011 年 1 月 -2012 年 1 月门诊诊治的 98 例 RA 患者分别采取双氯芬酸钠和塞来昔布治疗,现将研究结果报道如下。

1 资料与方法

1.1 一般资料

研究对象均为我院 2011 年 1 月 -2012 年 1 月风湿免疫科门诊诊治的类风湿性关节炎患者共 98 例,其中男性 25 例,女性 73 例,患者年龄均为 34-78 岁,病程均在 1-32 年。将所有患者随机分为两组,每组各 49 例,其中对照组中男性 12 例,女性 37 例,平均年龄为(60.36± 3.25)岁,平均病程为(8.65± 0.38)年,关节功能分级为Ⅰ级 18 例,Ⅱ级 16 例和Ⅲ级 15 例;观察组中男性 13 例,女性 36 例,平均年龄为(60.86± 3.52)岁,平均病程为(8.16± 0.33)年,关节功能分级为Ⅰ级 17 例,Ⅱ级 17 例和Ⅲ级 15 例。两组患者在性别、年龄、病程及关节功能分级等

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一般资料比较,均无显著性差异(P>0.05),具有可比较性。

1.2 诊断标准

患者临床诊断均符合 1987 年美国风湿病学学会(ARA)制定的类风湿关节炎诊断和分类标准[9,10],且经体格检查和临床、实验室指标确诊,其血清类风湿因子(RF)为阳性;晨僵时间≥ 1h 且持续 6 周以上;关节肿胀数≥ 3 个且持续 6 周以上;关节压痛≥ 5 个;红细胞沉降数(ESR)≥ 28 mm/h。患者均知情且签署治疗同意书。

1.3 排除标准

患者均排除:合并心、脑、肝、肾或血管及造血系统等原发性疾病患者;合并系统性红斑狼疮、膝骨关节炎或干燥综合征等其他免疫系统疾病患者;晚期出现严重强直、畸形或丧失劳动能力者; 近 3 个月内接受糖皮质激素或抗风湿药物治疗者; 伴有中枢神经系统损害者; 严重药物过敏或具有使用禁忌症者;恶性肿瘤患者;精神异常或意识障碍者;妊娠期或哺乳期妇女等。

1.4 治疗方法

两组患者均采取基础治疗,即:甲氨蝶呤(MTX)10mg/ 次, 1 次 / 周,饭后服用;羟氯喹(HCQ)200 mg/ 次,2 次 /d,口服;对照组患者在基础治疗基础上给予双氯芬酸钠缓释片 75mg/ 片, 1 片 /d,睡前口服,3 个月为 1 个疗程;观察组患者给予塞来昔布胶囊,200mg/ 粒,2 粒 /d, 于早晚分两次口服,3 个月为 1 个疗程。观察并比较两组临床治疗效果、血沉(ESR)、C 反应蛋白(CRP)及类风湿因子(RF)等实验室指标变化及心血管不良事件发生情况。

1.5 疗效判定

疗效判定标准为[11]:显效:患者临床症状和体征基本消失或改善≥ 75%,ESR 和 CRP 等实验室指标下降至正常或接近正常; 有效: 患者临床症状和体征改善在 30%-75%,ESR 和 CRP 等实验室指标明显下降; 无效: 患者临床症状和体征改善< 30%。总有效率 =(显效 + 有效)/ 总例数× 100%。

1.6 统计学方法

结果均采用 SPSS17.00 统计学软件处理, 计量资料以均数± 标准差($\bar{x}$± s)表示,组间比较采用两独立样本 t 检验,组内比较采用配对 t 检验;计数资料采用 x^2 检验,检验值 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

治疗 1 个疗程后观察组总有效率为 91.84%, 显著高于对照组的 75.51%,两组有效率比较具有显著性差异(P<0.05),结果详见表 1。

表 1 两组临床疗效比较(例,%)

Table 1 Comparison of clinical effect between two groups (n, %)

组别 Groups	例数 n	显效 Markedly	有效 Effective	无效 Invalid	总有效率(%) Total efficiency
对照组 Control group	49	17	20	12	37(75.51)
观察组 Observation group	49	24	21	4	45(91.84)[a]

注:与对照组比较,[a]P< 0.05。

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

2.2 两组治疗前后实验室指标变化比较

经统计学分析可知,两组治疗后 ESR 和 CRP 指标均较治疗前显著降低,其中观察组 ESR 和 CRP 分别为(110.65± 7.28) mm/h 和(10.42± 0.98)mg/L,较对照组降低更为显著,且差异均具有统计学意义(P<0.05),结果详见表 2。

表 2 两组治疗前后实验室指标变化比较($\bar{x}$± s)

Table 2 Comparison of index changes between two groups before and after the treatment ($\bar{x}$± s)

组别 Groups	时间 Time	例数 n	ESR(mm/h)	CRP (mg/L)
对照组 Control group	治疗前 Before treatment	49	54.65± 4.60	30.23± 2.15
	治疗后 After treatment		36.30± 3.85[b]	20.36± 1.85[b]
观察组 Observation group	治疗前 Before treatment	49	13.69± 2.12	29.56± 2.36
	治疗后 After treatment		110.65± 7.28[ab]	10.42± 0.98[ab]

注:与对照组比较,[a]P< 0.05,与治疗前比较,[b]P< 0.05。

Note: Compared with the control group, [a]P< 0.05, compared with pre-treatment, [b]P< 0.05.

2.3 两组心血管不良事件发生情况比较

由临床结果可知,两组主要心血管事件有高血压、心悸和心肌梗死等,其中观察组总发生率为 8.16%显著低于对照组的 20.41%,两组比较差异具有统计学意义(P<0.05),结果详见表 3。

表 3 两组心血管不良事件发生情况比较(例,%)

Table 3 Comparison of adverse cardiovascular events between the two groups (n, %)

组别 Groups	例数 n	高血压 Hypertension	心悸 Palpitations	心肌梗死 Myocardial infarction	发生率(%) Incidence (%)
对照组 Control group	49	6	3	1	10(20.41)
观察组 Observation group	49	3	1	0	4(8.16)[a]

注:与对照组比较,[a]P<0.05。

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

3 讨论

类风湿性关节炎(RA)是临床上的常见病、多发病,以关节滑膜炎为主要特征,主要累及周围关节,临床主要表现为受累关节的疼痛或肿胀、关节功能障碍等[12]。作为一种慢性多发性关节炎,患者病情成持续、反复的发作,且具有较高的致残率和致死率,对患者的身心健康和生命安全威胁较大,也是造成患者劳动力缺失和致残的主要原因之一[13,14]。目前对 RA 的病因尚未有明确的认识,但部分学者认为其与感染、遗传或免疫等有关,其中前列腺素在发病过程中发挥重要的作用[15]。目前临床治疗风湿性关节炎以来氟米特、甲氨蝶呤等免疫抑制剂及双氯芬酸钠和布洛芬等非甾体抗炎药物为主,其中免疫抑制剂的临床效果较慢,毒副作用较大且患者易产生耐药反应;而非甾体类抗炎药(non-steroidal anti-inflammatory drugs,NSAIDs)通过抑制环氧酶 COX 的活性,并阻断下游的前列腺素 E2 的产生而控制关节肿痛以发挥临床疗效,广泛应用于类风湿性关节炎、骨关节炎等多种免疫功能紊乱所致炎性疾病,但其以胃肠道损伤为主要毒副作用,严重者甚至引起胃肠道粘膜的病变而出现溃疡或出血,不利于患者的长期用药治疗[16,17]。

塞来昔布是一种高特异性的 COX2 抑制剂,通过阻止炎性前列腺素物质的生成而发挥抗炎、镇痛和解热作用,且无明显的胃肠道反应,可有效缓解 RA 患者的炎性症状和疼痛指数等[18-20]。本研究选取我院 2011 年 1 月 -2012 年 1 月收治的 RA 患者分别采取双氯芬酸钠和塞来昔布治疗,通过观察患者治疗前后临床症状改善及实验室指标变化可知,塞来昔布治疗类风湿性关节炎疗效显著,其有效率高达 91.84%,显著高于对照组,且观察组治疗后 ESR、CRP 及 RF 分别为(110.65± 7.28)mm/h、(10.42± 0.98)mg/L 和(42.36± 7.35)IU/mL,均较对照组降低更为显著(P<0.05),结果说明塞来昔布治疗类风湿性关节炎疗可明显改善患者临床症状,改善 ESR、CRP 及 RF 等实验室指标水平;而两组心血管不良事件主要有高血压、心悸和心肌梗死等,且观察组发生率显著低于对照组,差异具有统计学意义(P<0.05),结果说明塞来昔布治疗类风湿性关节炎疗安全性高,患者易耐受。

综上所述,塞来昔布治疗类风湿性关节炎疗具有较好的临床治疗效果,可明显改善患者疼痛、僵硬或功能受限等临床症状和体征,且心血管不良事件发生率低,安全性高,具有较好的临床应用价值,值得进一步推广和应用。

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