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奥沙利铂联合替吉奥胶囊治疗晚期大肠癌患者的临床疗效

张春侠 章来长 王 妍 赵胤铭 张晓元

（空军航空医学研究所附属医院普外科 北京 100089）

摘要 目的:探讨奥沙利铂联合替吉奥胶囊治疗晚期大肠癌患者的临床疗效。**方法:**非盲法随机对照方法将患者分成试验组和对照组,各27例。试验组患者使用奥沙利铂联合替吉奥胶囊治疗,对照组患者使用奥沙利铂治疗,均为4个周期。评价两组治疗后的临床疗效和不良反应。**结果:**试验组:CR 1例,PR 11例,SD 10例,PD 5例。(CR+PR)RR 44.4%。中位疾病进展时间(TTP)9.5个月,中位生存期(MST)19.1个月。对照组:CR 0例,PR 5例,SD 8例,PD 15例。(CR+PR)RR 18.5%。中位疾病进展时间(TTP)8.6个月,中位生存期(MST)16.9个月。主要不良反应为血液毒性、胃肠道反应、外周神经炎及肝功能异常。试验组白细胞下降15例,对照组12例,试验组贫血发生为13例,对照组的为21例,试验组恶心、呕吐发生为18例,对照组为24例,试验组便秘发生为8例,对照组为15例,差异有统计学意义(P<0.05)。**结论:**奥沙利铂联合替吉奥胶囊治疗晚期大肠癌患者相比单独使用奥沙利铂更加有效,更具优越性,不良反应更少,患者的生存质量得以改善,值得临床上推广应用。

关键词:奥沙利铂;替吉奥胶囊;晚期大肠癌

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Curative Effect of Oxaliplatin Combined with S-1 capsule in the Treatment of Advanced Colorectal Carcinoma

ZHANG Chun-xia, ZHANG Lai-chang, WANG Yan, ZHAO Ying-ming, ZHANG Xiao-yuan

(Department of general surgery, Air Force Aviation Medicine Research Institute affiliated hospital, Beijing, 100089, China)

ABSTRACT Objective: To evaluate the curative effect of oxaliplatin combined with S-1 capsule in the treatment of advanced colorectal carcinoma. **Methods:** Non-blinded randomized controlled trial was used, 27 cases were in the test group, and were treated with oxaliplatin combined with S-1 capsule; 27 cases which were only treated with oxaliplatin were in the control group. The curative effect and side effects were evaluated after 4 cycles of treatment. **Result:** Test group: CR was observed in 1 patient, PR in 11 patients, SD in 10 patients, and PD in 5 patients. The total effective rate was 44.4%. The median time to disease progression (TTP) were 9.5 months, median survival time (MST) were 19.1 months. Control group: CR was observed in no patient, PR in 9 patients,SD in 10 patients, and PD in 8 patients. The total effective rate was 18.5%. The median time to disease progression (TTP) was 8.6 months, and median survival time (MST) was 16.9 months. Major side effects were hematotoxicity, gastrointestinal reaction, peripheral neuritis and abnormal liver function. The leukopenia was found in 15 cases in the test group and in 12 cases in control group. The incidence of anemia in test group was 13 cases, in comparison with the 21 cases in control group. The incidence of nausea or vomiting in test group was 18 cases, in comparison with the 24 cases in control group. The incidence of constipation in test group was 8 cases,in comparison with the 15 cases in control group. The differences were statistically significant (P<0.05). **Conclusion:** Oxaliplatin combined with S-1 capsule is effective, advantageous and has lower side effects in comparison with using oxaliplatin alone in the treatment of patients with colorectal cancer. It can improve the life quality of the patients and is worthy of clinical application.

Key words: Oxaliplatin; S-1 capsule; Advanced colorectal carcinoma

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前言

随着人们生活质量的增加，大肠癌的发病率越来越高,其发病率仅次于胃癌和食管癌,已经成为常见的胃肠道恶性肿瘤之一[1-4]。由于其早起症状不明显,病情被发现一般已进入中晚期,手术治疗效果不显著[5-7],因此,化疗成为了治疗晚期大肠癌患者的主要手段之一,占据越来越重要的地位[8,9]。我科自2008年2月至2013年8月间共收治晚期大肠癌共54例,分别进行奥沙利铂联合替吉奥胶囊、奥沙利铂化疗,结果报告如下。

作者简介:张春侠(1973-),女,本科,主治医师,研究方向:乳腺肿瘤、大肠肿瘤方面,E-mail:zhangchunxia236@126.com

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1 资料与方法

1.1 一般资料

本组大肠癌晚期患者共54例,男性30例,女性24例,年龄35岁～77岁,全部病例均有病理学依据,被证实为直肠癌或者结肠癌晚期;其中初治患者15例,复治患者39例;直肠癌20例,结肠癌34例;非盲法随机分实验组与对照组各27例。复治患者曾接受过5-FU/CF、DDP等化疗，但跟上次化疗时隔

1 月以上;原发灶及转移灶均经 CT、MRI、B 超证实;预计生存期≥3 个月;体力状况评分(ECOG)0～2 分;无其他恶性肿瘤病史;无无外周感觉神经病变;无化疗相对及绝对禁忌症,血常规肝肾功能及心电图等检查大致正常。

1.2 治疗方法

试验组 27 例,奥沙利铂联合替吉奥胶囊,餐后口服替吉奥胶囊 80 mg/m^2,分 2 次,$d_{1\text{-}14}$,静脉滴注奥沙利铂 85 mg/m^2,3 h,d_1,28 天一周期;对照组 27 例,静脉滴注奥沙利铂 85 mg/m^2,3 h,d_1,静脉滴注亚叶酸钙 200 mg/m^2,2h,$d_{1\text{-}5}$,静脉滴注氟尿嘧啶 300 mg/m^2,2 h,$d_{1\text{-}5}$,28 天一周期,两组共 4 个周期。化疗前后检查血常规和肝肾功能。所有患者给予昂丹司琼等镇吐、维生素 B1、B6 等辅助治疗。嘱咐患者忌食冷饮及注意保暖。

1.3 评价标准

根据 WHO 实体瘤客观疗效评价标准,化疗 2 个周期后评价疗效,分为:完全缓解(CR),部分缓解(PR),稳定(SD),进展(PD)。用 CR+PR 计算有效率(RR)[10]。不良反应根据 WHO 抗癌药毒性分级标准,分为 0-Ⅳ级。疾病进展时间(TTP)为自化疗开始至疾病进展的时间[11,12]。

1.4 统计学处理

采用 SPSS17.0 软件进行统计学分析,两组均数比较采用 t 检验,计数资料比较采用卡方检验,等级资料如疗效、不良反应发生情况的比较采用秩和检验,生存率的比较采用 log-rank 检验,检验水准为 α=0.05。

2 结果

2.1 临床疗效

全组 54 例患者均化疗 4 个周期。试验组:CR 1 例,PR 11 例,SD 10 例,PD 5 例。(CR+PR)RR 44.4 %。中位疾病进展时间(TTP)9.5 个月,中位生存期(MST)19.1 个月。对照组:CR 0 例,PR 5 例,SD 8 例,PD 15 例。(CR+PR)RR 18.5 %。中位疾病进展时间(TTP)8.6 个月,中位生存期(MST)16.9 个月。试验组疗效、有效率、控制率均优于对照组,差异有统计学意义(P<0.05),试验组中位疾病进展时间、中位生存期长于对照组,差异有统计学意义(P<0.05)。

表 1 两组疗效比较(例)

Table 1 Comparison of curative effect of two groups(n)

组别 Groups	CR	PR	SD	PD	RR	TTP(月)	MST(月)
试验组(n=27) Test group(n=27)	1	11	12	3	12	9.5	19.1
对照组(n=27) Control group(n=27)	0	5	8	14	5	8.6	16.9
x^2		11.1685			4.207	10.126	15.563
P		0.011			0.040	0.000	0.000

2.2 不良反应

两组化疗方案, 在化疗期间主要不良反应为血液毒性、胃肠道反应、外周神经炎及肝功能异常等,试验组白细胞下降 15 例,对照组 12 例,试验组贫血发生为 13 例,对照组的为 21 例,试验组恶心、呕吐发生为 18 例,对照组为 24 例,试验组便秘发生为 8 例,对照组为 15 例,差异有统计学意义(P<0.05)。见表2。

表 2 两组之间不良反应情况比较

Table 2 Comparison of adverse reactions of the two groups

不良反应 Adverse reactions	试验组(n=27) Test group(n=27)						对照组(n=27) Control group(n=27)						x^2	P
	0	Ⅰ	Ⅱ	Ⅲ	Ⅳ	Ⅰ-Ⅳ	0	Ⅰ	Ⅱ	Ⅲ	Ⅳ	Ⅰ-Ⅳ		
白细胞减少 Leukopenia	12	5	8	2	0	15	5	9	8	5	0	22	4.207	0.040
贫血 Anemia	13	6	5	3	0	14	6	12	5	4	0	21	3.979	0.046
血小板下降 The decrease of platelet	11	8	6	2	0	16	9	9	6	3	0	18	0.318	0.573
恶心、呕吐 Nausea, vomiting	9	10	6	2	0	18	3	11	10	3	0	24	3.857	0.050
腹泻 Diarrhea	12	7	5	3	0	15	9	11	5	2	0	18	0.701	0.402
便秘 Constipation	19	6	2	0	0	8	12	13	2	0	0	15	4.472	0.034
外周神经炎 Peripheral neuritis	8	10	9	0	0	19	4	12	10	1	0	23	1.714	0.190
肝功能异常 Abnormal liver function	16	8	3	0	0	11	13	10	3	1	0	14	0.670	0.413

3 讨论

大肠癌是胃肠道中常见的恶性肿瘤之一,随着人们的生活质量越来越高,其发病率也在增加。大量临床实践和研究发现,大肠癌手术治疗效果不明显, 化疗是大肠癌治疗的主要手段,并且以全身化疗为主的综合治疗在改善病人的生活质量、延长生存期等方面的作用已被临床证实[13-15]。

奥沙利铂是第 3 代铂类抗癌药物, 以 DNA 为靶点,由

DNA 链与铂原子联合来阻碍 DNA 的转录与复制，其阻碍 DNA 合成与破坏 DNA 的结构和功能的联合应用形成互补抑制的协调效果。奥沙利铂的骨髓抑制、胃肠道反应均较顺铂轻，无肾毒性，抗癌谱更广。有研究表明，联合化疗对转移性与进展结直肠癌疗效明显，是当今结直肠癌治疗疗效最佳的药物之一[16]。替吉奥，是一种新型口服化疗药，为第 4 代氟尿嘧啶衍生物口服抗癌剂，其由两类调节剂奥替拉西及吉美嘧啶和替加氟组成，前两种成分起到共同抗肿瘤生化调节剂作用，使病人体内能够保持较高浓度较长时间的 5-FU 血药浓度，加强了 5-FU 的抗癌功效，同时减轻了毒副作用[17]。据文献报道，替吉奥胶囊一线治疗晚期大肠癌的 100 例患者中，有效率达到 36.5%。在中国，替吉奥是一线治疗胃癌的标准方案[18]。有研究显示，奥沙利铂联合替吉奥胶囊治疗晚期大肠癌患者疗效较好，可改善患者生存，降低复发[19,20]。

本研究采用奥沙利铂联合替吉奥胶囊治疗晚期大肠癌患者，比较奥沙利铂联合替吉奥胶囊及单用奥沙利铂效果的差别，结果显示：试验组有效率为（CR+PR）RR 44.4 % vs 对照组（CR+PR）RR 33.3 %，中位疾病进展时间（TTP）9.5 个月 vs 中位疾病进展时间（TTP）8.6 个月，中位生存期（MST）19.1 个月 vs 中位生存期（MST）16.9 个月，试验组较对照组显示有更好的疗效。试验组白细胞下降 15 例，对照组 12 例，试验组贫血发生为 13 例，对照组的为 21 例，试验组恶心、呕吐发生为 18 例，对照组为 24 例，试验组便秘发生为 8 例，对照组为 15 例，差异有统计学意义，对照组不良反应高于试验组。

综上，奥沙利铂联合替吉奥胶囊治疗晚期大肠癌患者相比单独使用奥沙利铂更加有效，更具优越性，不良反应更少，患者的生存质量得以改善，值得临床上推广应用。

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