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替吉奥联合伊立替康治疗晚期结肠癌的临床研究

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摘要 目的：比较替吉奥联合伊立替康与替吉奥单药治疗晚期结肠癌的临床疗效。**方法**：选取 2011 年 3 月～2012 年 3 月我院收治的晚期结肠癌患者 90 例，按照随机数字表法将患者分为研究组和对照组，每组 45 例，研究组给予替吉奥联合伊立替康，对照组给予替吉奥单药治疗，比较两组近期疗效、远期疗效和不良反应。**结果**：研究组的总有效率 51.1%(23/45)显著高于对照组的 26.7%(12/45)，两组比较差异具有统计学意义(X^2=13.281，P=0.017)；研究组中位进展时间和中位生存时间均显著长于对照组，两组比较差异具有统计学意义(t=9.029，10.412，P=0.021，0.019)；两组中性粒细胞减少和腹泻比较差异具有统计学意义(X^2=11.517，12.041；P=0.023，0.019)。**结论**：替吉奥联合伊立替康治疗晚期结肠癌较单用替吉奥具有更好的治疗效果，值得临床推广应用。

关键词：晚期结肠癌；替吉奥；伊立替康；疗效

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The Clinical Research of Gio Combined with Irinotecan in Treatment of Advanced Colorectal Cancer

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ABSTRACT Objective: To compare the clinical efficacy of Gio combined with irinotecan and monotherapy of Gio in treatment of advanced colorectal cancer. **Methods:** 90 cases of advanced colorectal cancer were selected from our hospital from March 2011 to March 2012, and they were divided into the study group and the control group according to the random number table, with 45 cases in each group. The study group were treated with Gio combined with irinotecan, and the control group were treated with Gio alone, the short-term effect, long-term efficacy and adverse reactions of two groups were compared. **Results:** The total efficiency of the study group was 51.1% (23/45), significantly higher than 26.7% (12/45) of the control group, and the difference was statistically significant (X^2=13.281, P=0.017); The median progression time and median survival time of the study group were significantly longer than those of the control group, the differences were statistically significant (t=9.029, 10.412, P=0.021, 0.019); Incidence of Neutropenia and diarrhea of the two groups showed statistically significant difference(X^2=11.517, 12.041; P=0.023, 0.019). **Conclusion:** Gio combined with irinotecan had better efficacy in treatment of advanced colorectal cancer when compared with mono-therapy of Gio. It is worthy of clinical application.

Key words: Advanced colorectal cancer; Gio; Irinotecan monotherapy; Efficacy

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前言

结肠癌是常见的恶性肿瘤之一，化疗是晚期结肠癌治疗的主要方法[1]，其中氟尿嘧啶是治疗结肠癌的基础，替吉奥的主要成分为氟尿嘧啶衍生物[2]。许多研究发现，替吉奥联合伊立替康化疗用药晚期结肠癌的治疗具有较满意的效果，且两种药物联合用药较方便，可以显著改善患者临床症状，减少住院时间，进而延长患者的生命[3,4]。本研究旨在比较替吉奥联合伊立替康与替吉奥单药治疗晚期结肠癌的临床疗效，现将结果报告如下。

1 资料与方法

1.1 一般资料

选取 2011 年 3 月～2012 年 3 月我院收治的晚期结肠癌患者 90 例，所有患者均经病理确诊为复发或者转移的晚期患者。且预计生产期超过 12 周，既往未应用化疗或者辅助化疗治疗，并排除严重内科或者外科疾病，其他恶性肿瘤病史者、脑转移或者肝脏转移。按照随机数字表法将患者分为研究组和对照组，各 45 例。研究组男性 27 例，女性 18 例；年龄 37～75 岁，平均年龄(56.3± 0.8)岁。对照组男性 26 例，女性 19 例，年龄 36～75 岁；平均年龄(57.2± 1.1)岁。两组患者的年龄和性别比较均无显著差异(P＞0.05)，具有可比性，研究经伦理委员会批准，所有患者均知情同意并签订知情同意书。

1.2 治疗方法

研究组：给予患者伊立替康(生产厂家：Aventis Pharma Dagenham，生产批号：H20090659)150 mg/m^2 加入到 250 mL 生理盐水中静脉滴注，替吉奥(生产厂家：山东新时代药业有限公司，生产批号：国药准字 H20080802)80 mg/d(面积小于 1.25

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m^2)、100mg/d(面积介于 1.25-1.5 m^2)和 120 mg/d(面积大于 1.5 m^2),分 2 次服用,餐后服用,连续应用 14 d,间隔 7 天,为 1 个疗程。对照组:给予患者替吉奥,用法用量均与研究组相同。两组均应用药物直到病情进展或者是不良反应不可耐受,且最多进行 8 个疗程治疗。

1.3 疗效评价

近期疗效根据 WHO 关于实体肿瘤客观疗效评价标准来评价[5]:完全缓解(CR):是指所有可以测量的病灶均消失;部分缓解(PR):是指双径可以测量的病灶的最大两个垂直直径的乘积总和缩小超过 50%;稳定(SD):是指减少少于 50%或者是增大超过小于 25%,且无新病灶;病情进展(PD):是指增大超过 25%或者是出现新的病灶。(总有效 =CR+PR)。

1.4 统计学方法

全部数据均在 SPSS17.0 软件上统计,其中计量资料用($\bar{X}\pm S$)表示,应用 t 检验,计数资料应用 X^2 检验,检验标准以 $P<0.05$ 表示有统计学意义。

2 结果

2.1 两组近期疗效比较

由表 1 可知,研究组的总有效率 51.1%(23/45)显著高于对照组的 26.7%(12/45),两组比较差异具有统计学意义(X^2=13.281,P=0.017)。

表 1 两组近期疗效比较[n(%)]

Table 1 Comparison of the short-term effect between two groups[n(%)]

组别 Groups	例数 Cases	CR	PR	SD	PD	总有效 Total efficiency
对照组 Control group	45	5(11.1)	7(15.6)	18(40.0)	15(33.3)	12(26.7)
研究组 Study group	45	11(24.4)	12(26.7)	13(28.9)	9(20.0)	23(51.1)[a]

注:与对照组比较,X^2=13.281,[a]P=0.017。

Note:compared with control group,X^2=13.281,[a]P=0.017.

2.2 两组远期疗效比较

由表 2 可知,研究组中位进展时间和中位生存时间均显著长于对照组,两组比较差异具有统计学意义(t=9.029,10.412,P=0.021,0.019)。

表 2 两组远期疗效比较(月,$\bar{x}\pm s$)

Table 2 Comparison of long-term efficacy between two groups(month,$\bar{x}\pm s$)

组别 Groups	中位进展时间 Median progression time	中位生存时间 Median survival time
对照组 Control group	4.5± 0.4	3.1± 0.8
研究组 Study group	7.2± 0.3a	17.3± 1.3a

注:与对照组比较,t=9.029,10.412,[a]P=0.021,0.019。

Note: compared with control group, t=9.029, 10.412, [a]P=0.021, 0.019.

2.3 两组不良反应比较

研究组恶心呕吐 11 例,腹泻 5 例,中性粒细胞减少 5 例,乏力 7 例,对照组不良反应轻微,恶心呕吐 12 例,腹泻 2 例,中性粒细胞减少 1 例,乏力 8 例,两组中性粒细胞减少和腹泻比较差异具有统计学意义(X^2=11.517,12.041;P=0.023,0.019)。

3 讨论

晚期结肠癌患者预后一般比较差,全身化疗是治疗的主要方法,能显著改善患者的生活质量,延长其生存时间,氟尿嘧啶联合伊立替康用于晚期结肠癌的治疗,并且其临床效果较好,已经取得国际上的认可,成为标准的治疗方案之一[6-8]。随着人们对药物安全性和治疗依从性的关注度的增加,促使临床研发新型的口服氟尿嘧啶。替吉奥是一种新型口服制剂,是氟尿嘧啶的衍生物,主要由替加氟、奥替拉西钾和吉美嘧啶构成,口服以后替加氟可以在人体内缓慢的转变成 5- 氟尿嘧啶,起到抗肿瘤的作用[9]。替加氟还可以抑制胸苷酸合成酶,进而抑制脱氧尿苷酸,起到扰乱 DNA 合成的作用。吉美嘧啶主要分布于肝脏中,对 5- 氟尿嘧啶的代谢酶具有拮抗作用,进而增加 5- 氟尿嘧啶的浓度,增强其抗肿瘤的作用。该物质还可以减少 5- 氟尿嘧啶的代谢产物,进而减少其带来的副作用。奥替拉西钾口服以后可以选择性的分布在结肠和小肠,可以选择性的抑制 5- 氟尿嘧啶转化成 5-FU MP,进而加强药物的抗癌作用[10-13]。

伊立替康是一种 DNA 的拓扑异构酶 I 的抑制剂,可以诱导 DAN 单链发生破坏,进而阻断 DNA 的复制叉,使 DNA 的两条链重组受到阻碍,导致双链发生断裂,引起细胞死亡,最终起到治疗肿瘤的作用[14-16]。有研究显示,伊立替康单独治疗晚期结肠癌的有效率大约为 29%,伊立替康和氟尿嘧啶具有协同作用,而且不具有交叉耐药性[17]。本研究发现,研究组的总有效率 51.1%(23/45)显著高于对照组的 26.7%(12/45),与相关研究结果一致[4,17],充分证实替吉奥联合伊立替康治疗晚期结肠癌相

比替吉奥单用效果好,能显著缓解患者的临床症状。且中位进展时间和中位生存时间均显著长于对照组,说明其远期疗效优越。伊立替康存在一定的不良反应,据研究[18,19],其不良反应主要表现为中性粒细胞减少和迟发型的腹泻,迟发型的腹泻主要是剂量限制性的不良反应。该药物的消化道毒性较小。本研究发现,研究组恶心呕吐 11 例,腹泻 5 例,中性粒细胞减少 5 例,乏力 7 例,对照组不良反应轻微,恶心呕吐 12 例,腹泻 2 例,中性粒细胞减少 1 例,乏力 8 例,两组中性粒细胞减少和腹泻比较差异具有统计学意义,与 Wissing MD 等人研究结果一致[20]。

综上所述,替吉奥联合伊立替康治疗晚期结肠癌相比替吉抗单药治疗具有较好的近期疗效和远期疗效, 且用药方便,可以作为化学治疗的优化方案。但本研究的例数相对较少,需要继续扩大研究,进而为临床提供有利的证据。

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