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替吉奥联合奥沙利铂及多西紫杉醇治疗晚期胃癌的临床疗效和安全性评估*

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摘要 目的:观察替吉奥联合奥沙利铂及多西紫杉醇治疗晚期胃癌的近期疗效,并对其用药安全性进行评估。**方法:**选取 2010 年 8 月—2012 年 8 月在我院接受治疗的晚期胃癌患者 68 例,随机分为对照组和观察组,每组 34 例。对照组患者采取 5-FU+奥沙利铂+多西紫杉醇进行治疗,而观察组患者给予替吉奥+奥沙利铂+多西紫杉醇进行治疗,比较两组患者接受不同药物治疗所得到的近期疗效及不良反应的发生情况。**结果:**观察组治疗的总有效率为 58.82%,而对照组治疗的总有效率为 32.35%,观察组明显高于对照组,差异显著,具有统计学意义($P<0.05$);观察组患者治疗后的不良反应发生率为 8.82%,而对照组患者治疗后的不良反应发生率为 32.35%,观察组明显低于对照组,差异显著,具有统计学意义($P<0.05$)。**结论:**替吉奥联合奥沙利铂及多西紫杉醇治疗晚期胃癌疗效显著,不良反应少,患者耐受良好,值得进一步推广和应用。

关键词:替吉奥;奥沙利铂;多西紫杉醇;晚期胃癌

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Clinical Efficacy and Security Evaluation on Tegafur Combined with Oxaliplatin and Docetaxel for the Treatment of Advanced Gastric Cancer*

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ABSTRACT Objective: To explore the clinical efficacy and security of tegafur combined with oxaliplatin and docetaxel on the treatment of advanced gastric cancer. **Methods:** 68 patients with advanced gastric cancer who were treated in our hospital from August 2010 to 2012 were selected and randomly divided into the observation group and the control group with 34 patients in each group. The patients in the control group were treated by 5-FU+oxaliplatin+docetaxel, while the patients in the observation group were treated by Gio+oxaliplatin +docetaxel. Then the short-term efficacy and adverse reactions of patients were compared and analyzed between two groups. **Results:** The effective rate of the observation group was 58.82%, while the effective rate of the control group was 32.35%. The observation group was statistically significant higher than the control group ($P<0.05$). The incidence of adverse reactions in the observation group was 8.82% which was lower than that of the control group 32.35%. There was statistically significant difference between two groups($P<0.05$). **Conclusion:** It is suggested that the tegafur combined with oxaliplatin and docetaxel on the treatment of advanced gastric cancer should be well promoted in the clinical field with the advantages of obvious efficacy, less incidence of adverse reactions and easier adopted by patients.

Key words: Tegafur; Oxaliplatin; Docetaxel; Advanced gastric cancer

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前言

胃癌(Gastric cancer)是临床上较为常见的消化道恶性肿瘤之一,在中国其发病率居各类肿瘤的首位,每年约有 17 万人死于胃癌,几乎接近全部恶性肿瘤死亡人数的 1/4,且每年还有 2 万以上的人被确诊为胃癌^[1,2]。近年来,随着人们生活水平的不断提高及人口老龄化问题逐渐严重,胃癌的发病率和死亡率也随之明显提高,严重威胁人类的身心健康和生命安全^[3]。胃癌起

源于胃壁最表层的粘膜上皮细胞,可发生于胃的各个部位,以胃窦幽门区最多,胃底贲门区次之,胃体部略少。癌灶局限在粘膜内或粘膜下层的称为早期胃癌,侵犯肌层以深或有转移到胃以外区域者称为进展期胃癌,即晚期胃癌^[4-6]。胃癌发病早期临床症状不明显,缺乏特异性,因此对该病的早期确诊率极低,大多数患者就诊时已发展为胃癌晚期,错过了采取手术治疗的最佳时机^[7,8]。目前,临床多采取化疗的方法对胃癌患者进行治疗,但化疗产生的不良反应多,患者难以耐受。因此,寻找一种相对

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安全且有效的化疗方案成为临床关注的重点^[9,10]。本研究对我院 2010 年 8 月-2012 年 8 月收治的晚期胃癌患者实施不同的化疗方案,探讨临床疗效及用药安全性,现将研究结果报道如下:

1 资料与方法

1.1 一般资料

选取我院 2010 年 8 月-2012 年 8 月收治的晚期胃癌患者 68 例,其中男性 37 例,女性 31 例,年龄均在 41-81 岁,初治 33 例,复治 35 例。随机分为两组,每组各 34 例。对照组中,男性 18 例,女性 16 例,平均年龄为(58.44±4.23)岁,低分化癌 16 例,中分化癌 14 例,黏液腺癌 4 例;观察组中,男性 19 例,女性 15 例,平均年龄为(59.01±4.36)岁,低分化癌 17 例,中分化癌 13 例,黏液腺癌 4 例。两组患者在性别、年龄、病情及病理类型等一般资料方面无显著差异,具有可比性。

1.2 入选标准

患者均经病理组织及影像学检查确诊为晚期胃癌,按照国际 TNM 分期为 III-IV 期,具有 1 个或以上可测量病灶,KPS 评分均>60 分,且预计生存期>3 个月。所有患者均无化疗药物禁忌症,且经家属或患者同意并签署知情同意书。

1.3 治疗方法

对照组:5-FU 2400 mg/m², 静脉滴注, d₁₋₅, 奥沙利铂 130

mg/m², 静脉滴注 2h, d₁; 多西紫杉醇 60 mg/m², 静脉滴注 1h, d₁。观察组:替吉奥胶囊 80 mg/(m²·d), 分两次口服, d₁₋₁₄; 其余同对照组。比较两组临床疗效及不良反应发生情况。

1.4 疗效判定

依据 WHO 制定的抗肿瘤药物疗效判定标准:完全缓解(CR),部分缓解(PR),稳定(SD),进展(PD);有效率 RR=(CR+PR)/总例数×100%;不良反应参照 WHO 毒副反应分级标准。

1.5 统计学方法

采用 SPSS17.0 统计学软件处理,各组指标以均数±标准差($\bar{x} \pm s$)表示,进行 t 检验;而计数资料采用 χ^2 检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组患者的近期疗效比较

治疗后,观察组中全部缓解 2 例,部分缓解 18 例,病情稳定 8 例,病情有所进展 6 例,治疗的总有效率为 58.82%;对照组中无一例全部缓解,部分缓解 11 例,病情稳定 14 例,病情有所进展 9 例,治疗的总有效率为 32.35%。观察组的近期疗效明显高于对照组,两组比较差异显著,具有统计学意义(P<0.05),见表 1。

表 1 两组近期疗效比较

Table 1 Comparison of the short-term efficacy of patients between two groups

Groups	Cases	Complete Remission	Partial remission	Stable	Progress	Effective rate
Control	34	0	11	14	9	32.35%
Observation	34	2	18	8	6	58.82% ^a

Note: Compared with control group, aP<0.05.

2.2 两组患者的不良反应发生情况

化疗的主要不良反应为胃肠道反应、神经毒性、骨髓抑制等。本组不良反应均为 I-II 级,经对症处理后有明显好转或消失。观察组治疗后出现腹泻的有 1 例,恶心呕吐的 1 例,骨髓抑制 1 例,无白细胞减少或周围神经毒性病变发生,不良反应发

生率为 8.82%;对照组治疗后出现腹泻的有 2 例,恶心呕吐的 2 例,骨髓抑制 1 例,白细胞减少 2 例,周围神经毒性病变 3 例,不良反应发生率为 32.35%。观察组明显优于对照组,两组比较差异显著,具有统计学意义(P<0.05),见表 2。

表 2 两组不良反应发生情况比较

Table 2 Comparison of the incidence of complications between two groups

Groups	Cases	Diarrhea	Diarrhea/vomit	Myelosuppression	Leukopenia	Toxicity of surrounding nerve	Incidence of complication
Control	34	3	2	1	2	3	32.35%
Observation	34	1	1	1	0	0	8.82% ^a

Note: Compared with control group, aP<0.05.

3 讨论

在我国,胃癌是发病率较高的一种恶性肿瘤,且死亡率极高。患者早期临床症状不明显,就诊时多已进展为晚期,丧失根治手术的机会,其 5 年生存率不足 20%^[11-13]。另外,有一部分患者在手术后易发生癌细胞扩散或转移,严重威胁生命安全^[14]。

目前,晚期胃癌患者的临床治疗主要手段是放化疗,该方法在一定程度上可延长患者生命,提高生活质量^[15]。目前临床尚无公认的“金标准”化疗方案,那么合理选择既安全又有效的化疗药物,使其发挥最大效能,减少不良反应的发生是目前临床肿瘤研究领域关注的重点^[16]。一直以来,5-FU 作为临床治疗消化道肿瘤的核心药物,其单用药有效率达 20%左右,但药物半

衰期短、药效持续时间短、且不良反应多,在临床应用中受到一定的限制^[17]。

替吉奥(S-1)是新一代的 5- 氟尿嘧啶衍生物,由替加氟(FT),吉美嘧啶(gime racil,CDHP),奥替拉西钾(oteracil potassium,OXO)两种生化修饰剂按照摩尔比值 1:0.4:1 制成的复方制剂,也是一种增效减毒的改良制剂。其中,替加氟为 5- 氟尿嘧啶的前体药物,可在体内阻断 RNA、DNA 及蛋白质的合成,发挥抗肿瘤作用,其口服吸收后转化为 5- 氟尿嘧啶,生物利用度高、药物半衰期长,疗效明显提高,且毒副作用低,具有较好的临床应用价值^[18]。吉美嘧啶可抑制二氢嘧啶脱氢酶的活性,以阻止 5- 氟尿嘧啶的降解,从而较长时间的保持血液或肿瘤组织中 5- 氟尿嘧啶的药物浓度,提高药物的抗癌活性,能够有效降低药物不良反应的发生;奥替拉西钾可特异性抑制肠道黏膜细胞乳清酸核糖转移酶的活性,从而阻断 5- 氟尿嘧啶的磷酸化,减少胃肠道不良反应的发生。因此,替吉奥与 5- 氟尿嘧啶相比可更好的维持高水平的血药浓度,同时可提高抗肿瘤活性及降低药物不良反应^[19]。奥沙利铂是第 3 代铂类化疗药物,抗癌活性强,对多种肿瘤细胞具有明显的抑制作用,且与顺铂等药物无交叉耐药性;多西紫杉醇可作用于细胞微管,通过促进其聚合、抑制其解聚重组而发挥疗效,具有抗肿瘤作用^[20]。

综上所述,本研究采用替吉奥联合奥沙利铂及多西紫杉醇治疗,有效率达 58.82%,且胃肠道反应、神经毒性、骨髓抑制等发生率低。说明,替吉奥联合奥沙利铂及多西紫杉醇治疗晚期胃癌效果显著,患者耐受良好,且不良反应少,值得临床进一步推广和应用。

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