

替吉奥联合顺铂治疗晚期胃癌临床疗效研究

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摘要 目的:研究替吉奥联合顺铂治疗晚期胃癌的疗效和安全性。**方法:**42例晚期胃腺癌患者随机分为观察组(21例)与对照组(21例)两组,观察组采用替吉奥联合顺铂,对照组采用卡培他滨联合顺铂。**结果:**两组患者疗效间差异无统计学意义($P>0.05$)。两组的不良反应主要为骨髓抑制、消化道反应和乏力,观察组Ⅲ度血小板减少发生率显著低于对照组($P<0.05$),Ⅲ度手足综合征的发生率亦显著低于对照组($P<0.05$)。**结论:**替吉奥联合顺铂治疗晚期胃癌疗效与卡培他滨联合顺铂相当,但其患者耐受性更好,值得临床进一步研究推广使用。

关键词:胃肿瘤;替吉奥;卡培他滨;顺铂;治疗结果

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Curative Effect Analysis of S-1 Combined with Cisplatin in the Treatment of Advanced Gastric Cancer

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ABSTRACT Objective: To investigate the safety and efficacy of S-1 combined with cisplatin in the treatment for patients with advanced gastric cancer. **Methods:** Forty-two patients with advanced gastric cancer were randomly divided into two groups. Patients in observation group ($n=21$) received S-1 and cisplatin; Patients in control group ($n=21$) received capecitabine and cisplatin. **Results:** The efficacy of the two groups showed no statistically significant difference ($P>0.05$). The main untoward effects were myelosuppression, gastroenteric reaction and weakness. Observation group showed a lower rate of untoward effects than control group. Observation group also showed a lower rate of Ⅲ degree thrombocytopenia ($P<0.05$) and hand-foot syndrome ($P<0.05$) than control group. **Conclusions:** The treatment of the two groups were evidently effective, with observation group having better tolerance. The regimen could be clinically recommended.

Key words: Stomach neoplasms; S-1; Capecitabine; Cisplatin; Treatment outcome

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前言

胃癌是我国最常见的恶性肿瘤之一,可发生于任何年龄,但以40~60岁多见,男性患者多于女性患者^[1-2]。胃癌的发病率居各类肿瘤的首位,每年死于胃癌的人数约占全部恶性肿瘤死亡人数的1/4,是一种严重威胁人民身体健康的疾病^[3-4]。大部分胃癌患者确诊时已处于中晚期,失去手术机会。化疗是治疗晚期胃癌的重要手段^[5-7]。2009年1月-2011年12月我院采用替吉奥联合顺铂(SP)治疗晚期胃癌,并与卡培他滨联合顺铂(XP)相比较,现将其疗效与安全性报告如下。

1 资料与方法

1.1 一般资料

2009年1月-2011年10月在我院住院治疗的晚期胃癌患者42例。其中男28例,女14例。年龄39~67岁,平均 (53.5 ± 7.5) 岁。42例患者B期12例,期30例;淋巴结转移21例,肝转移13例,肺转移7例,骨转移1例。所有患者均经病理学

确诊为晚期胃癌,并且为初次治疗。所有患者血常规、肝肾功能正常。均签署知情同意书。42例患者随机分为观察组(21例)与对照组(21例)两组。两组患者年龄、性别、疾病情况等一般资料没有显著差异,具有可比性($P>0.05$)。

1.2 治疗方法

观察组:替吉奥联合顺铂(SP)。口服替吉奥,用量 $40\text{ mg}\cdot\text{m}^2$,一日两次,饭后服用,连续服用14天。顺铂用量为 $75\text{ mg}/\text{m}^2$,化疗周期第一天内静脉滴注。对照组:卡培他滨联合顺铂(XP)。卡培他滨用量 $10000\text{ mg}\cdot\text{m}^2$,一日两次,连续服用14天。顺铂用量为 $75\text{ mg}/\text{m}^2$,化疗周期第一天内静脉滴注。21天为一个化疗周期。所有患者化疗期间给予地塞米松以预防胃肠反应,同时应用保护肝肾功能的药物。所有患者接受6个化疗周期。

1.3 疗效判定

患者疗效按RECIST标准分为完全缓解(CR)、部分缓解(PR)、稳定(SD)和进展(PD),完全缓解(CR)+部分缓解(PR)为有效。不良反应按照美国癌症研究所化疗毒性分级标准(CTC)进行判断,分为0~度。

1.4 统计学处理

数据采用SPSS13.0软件进行处理。 $P<0.05$ 为差异有统计

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学意义。

两组患者疗效情况见表 1。观察组总有效人数为 11 例,总有效率为 52.4%,对照组总有效人数为 10 例,总有效率为 47.6%,两组相比差异无统计学意义($P>0.05$)。

2 结果

2.1 两组患者疗效比较

表 1 两组患者临床疗效比较

Table 1 Comparison of the clinical efficacy of two groups of patients

组别 Groups	例数 Cases	CR	PR	SD	PD	总有效率 Total effective rate
观察组 Observation group	21	2	9	5	5	52.4%
对照组 Control group	21	1	9	5	6	47.6%

2.2 两组患者不良反应发生情况

均显著低于对照组,差异具有显著性($P<0.05$)。两组患者其余不良反应发生率组间比较差异无统计学意义($P>0.05$)。

患者的不良反应主要为骨髓抑制、消化道反应和乏力,观察组 ~ 度血小板减少发生率、 ~ 度手足综合征发生率

表 2 两组患者不良反应发生情况

Table 2 The adverse events of two groups of patients

不良反应 Adverse events	观察组(n=21) Observation group		对照组(n=21) Control group	
	~	~	~	~
中性粒细胞减少 Neutropenia	7	4	7	4
血红蛋白减少 Hemoglobin reduce	6	3	4	4
血小板减少 Thrombocytopenia	1	1	3	5
粒细胞减少性发热 Neutropenic fever	0	1	1	0
乏力 Fatigue	3	3	4	2
恶心呕吐 Nausea and vomiting	6	3	5	3
腹泻 Diarrhea	3	1	4	1
口腔炎 Stomatitis	5	1	6	1
手足综合征 Hand-foot syndrome	1	1	5	7
转氨酶升高 Elevated transaminase	3	0	2	1
肾功能损害 Impaired renal function	1	0	1	0

3 讨论

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(胃窦幽门区最多、胃底贲门区次之、胃体部略少),可侵犯胃壁的不同深度和广度。在消化系统恶性肿瘤死亡病例中,约半数死于胃癌^[8-9]。胃癌疗效与病期早晚和诊治方法及手段密切相关^[10-11]。胃癌的病因尚未完全清楚,目前认为与下列因素有关:(1)幽梦螺杆菌感染。胃癌高发区人群幽门螺杆菌感染率高。幽门螺杆菌能促使硝酸盐转化成亚硝酸盐及亚硝胺而致癌,幽门螺杆菌感染引起胃粘膜慢性炎症并通过加速粘膜上皮细胞的过度增殖导致畸变致癌;幽门螺杆菌的毒性产物 CagA、VacA 可能具有促癌作用^[12-13]。(2)癌前病变和癌前状态。胃癌的癌前病变有慢性萎缩性胃炎、胃息肉、胃溃疡及残胃炎,这些病变

常伴有不同程度的长期慢性炎症过程、胃粘膜肠上皮化生或非典型增生。胃粘膜上皮细胞的异型增生属于癌前病变,重度异型增生中有 75%~80%的病人有可能发展成胃癌^[14-15]。(3)遗传因素。胃癌有明显的家庭聚集倾向,有胃癌家族史者的发病率高于普通人群 2~3 倍。

化疗是晚期最主要的辅助治疗方法,目的在于杀灭残留的微小癌灶或术中脱落的癌细胞,提高综合治疗效果。替吉奥是一种氟尿嘧啶衍生物口服抗癌剂,它包括替加氟(FT)、吉美嘧啶(CDHP)及奥替拉西(Oxo)^[16-18]。其三种组分的作用如下:FT 是 5-Fu 的前体药物,具有优良的口服生物利用度,能在活体内转化为 5-Fu。CDHP 能够抑制在二氢嘧啶脱氢酶作用下从 FT 释放出来的 5-Fu 的分解代谢,有助于长时间血中和肿瘤组织中 5-Fu 有效深度,从而取得与 5-Fu 持续静脉输注类似的疗

效。Oxo 能够阻断 5-Fu 的磷酸化,口服给药之后,Oxo 在胃肠组织中具有很高的分布浓度,从而影响 5-Fu 在胃肠道的分布,进而降低 5-Fu 毒性的作用^[19-20]。替吉奥与 5-Fu 相比具有以下优势:①能维持较高的血药浓度并提高抗癌活性;②明显减少药毒性;③给药方便。多年的临床应用证明,替吉奥是安全有效的抗癌药物^[21]。据统计,日本目前晚期胃癌的化疗,有 80%以上的病例使用替吉奥,治疗有效率(CR+PR)可达 44.6%。

本研究显示,替吉奥联合顺铂(SP)治疗晚期胃癌与卡培他滨联合顺铂(XP)相比,临床效果无显著差异,这可能与样本量较少有关,需要进一步进行大样本研究。从不良反应发生情况来看,采用替吉奥联合顺铂,患者耐受性更好。

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