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吉西他滨联合化疗方案治疗复发转移性乳腺癌的临床疗效观察

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摘要 目的:观察吉西他滨与顺铂联合以及吉西他滨与紫杉醇联合治疗复发转移性乳腺癌的疗效和不良反应。**方法:**本研究收集65例女性乳腺癌术后复发转移的患者作为研究对象。随机分成两组,分别应用吉西他滨与顺铂(GP方案组)、吉西他滨与紫杉醇(GT方案组)联合进行治疗。GP方案组患者有30例,第1天、第8天用吉西他滨800mg~1000mg/m²溶于0.9%的100mL生理盐水中静脉滴注;第1天~第3天,21天重复用顺铂30mg/m²溶于0.9%的250mL生理盐水中静脉滴注;GT方案组患者有35例,吉西他滨的使用方法与GP方案组相同,第2天,21天重复用紫杉醇135mg/m²溶于0.9%的500mL生理盐水中静脉滴注。对化疗时产生的不良反应进行对症处理。**结果:**GP方案组化疗有效率为46.67%,疾病控制率为70.00%;GT方案组化疗有效率为42.86%,疾病控制率为68.57%,两组比较差异均无统计学意义($P>0.05$)。GT组脱发的发生率为62.86%,明显高于GP组的10.00%($P<0.001$),其他不良反应在两组之间差异无统计学意义($P>0.05$)。**结论:**GP方案和GT方案在治疗复发转移性乳腺癌有较好的疗效,不良反应较轻,可作为复方转移性乳腺癌的一种化疗方案。

关键词:吉西他滨;复发转移;乳腺癌**中图分类号:**R737.9 **文献标识码:**A **文章编号:**1673-6273(2014)05-917-04

Clinical Observation of Chemotherapy Regimen Based on Gemcitabine in the Treatment of Metastasis Breast Cancer

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ABSTRACT Objective: To compare the efficacy and side effects of GP and GT regimen in the treatment of metastasis breast cancer. **Methods:** We collected 65 cases of female patients with metastasis breast cancer as research subjects, which were randomly divided into two groups and jointly treated with GP regimen or GT regimen. There were 30 cases of patients in GP regimen group which were injected with Gemcitabine 800mg ~ 1000mg/m² dissolved in 0.9% saline infusion 100ml in day 1 and day 8, with Cisplatin 30mg/m² dissolved in 0.9% saline infusion 250 mL in other days; There were 35 cases of patients in GT regimen group which were injected with Gemcitabine 800mg ~ 1000mg/m² dissolved in 0.9% saline infusion 100ml in day 1 and day 8, with taxol 135mg/m² dissolved in 0.9% saline infusion 500ml in other days. Take expectant treatment when patients have side effects. **Results:** The efficiency of chemotherapy in GP regimen group was 46.67% and 42.86% in GT regimen group, the disease control rate in GP regimen group was 70.00% and 68.57% in GT regimen group, the difference was all not statistically significant($P>0.05$). The incidence of alopecia in GT regimen group was 62.86%, significantly higher than 10.00% in GP regimen group ($P<0.001$), Other side effects between the two groups showed no significant difference ($P>0.05$). **Conclusion:** GP and GT regimen are both effective in the treatment of metastasis breast cancer, and also, they both have mild side effects.

Key words: Gemcitabine; Metastasis; Breast cancer**Chinese Library Classification(CLC):** R737.9 **Document code:** A**Article ID:** 1673-6273(2014)05-917-04

前言

乳腺癌是影响到我国女性健康的十大肿瘤之一。近年来,发病率逐年升高,成为导致妇女死亡的主要恶性肿瘤^[1,2]。而在我国,乳腺癌的发病率快速增长,远高于世界的平均水平^[3,4]。目前对乳腺癌的临床治疗,主要是通过手术、化疗、放疗、靶向治疗等方法,化学药物治疗主要是应用蒽环类药物、紫杉类药物、氟尿嘧啶类药物,使得患者在临床化疗中得到较好的疗效^[5,6]。

但是对上述药物治疗后乳腺癌发生复发、转移,临床并未有公认的治疗方案。研究表明,吉西他滨对乳腺癌有明显的治疗效果^[7,8]。本研究选用吉西他滨与顺铂联合(简称GP方案)或者吉西他滨与紫杉醇联合(简称GT方案)治疗复发转移性乳腺癌,探讨其临床疗效,以期为复发转移性乳腺癌提供新的化疗方案。

1 资料与方法

1.1 一般资料

本研究收集65例女性乳腺癌术后复发转移的患者,经术后病理分析证实为乳腺浸润性导管癌,年龄为36~67岁,平均为44.2岁。随机分成两组,GP方案组30例,GT方案组35例,分别应用吉西他滨与顺铂联合、吉西他滨与紫杉醇联合进行治

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疗。原发病灶均进行过乳腺癌根治术,术后给予与蒽环类、紫杉醇类药物治疗,患者KPS评分均在60分以上,并且行其他常规

检查均显示正常,无化疗禁忌,见表1。

表1 两组患者一般情况比较(n)

Table 1 Comparison of general situations between the two groups

项目 Items		总例数 Total cases	GP 方案组 GP regimen group	GT 方案组 GT regimen group
年龄 Age	<50 years ≥ 50 years	48 17	22 8	26 9
月经状态 Menstrual status	绝经前 Premenopausal 绝经后 Postmenopausal	31 34	15 15	16 19
既往治疗 Previous treatment	单用蒽环类 Anthracycline alone 蒽环类联合紫杉类 Anthracyclineal combine with Taxane	25 40	12 18	13 22
骨转移 Bone metastases	Yes No	40 25	17 13	23 12
内脏转移 Visceral metastases	Yes No	31 34	16 14	15 20
转移灶 Metastases	<2 ≥ 2	28 37	12 18	16 19

1.2 治疗方案

GP方案组患者有30例,第1天、第8天用吉西他滨800mg~1000mg/m²溶于0.9%的100mL生理盐水中静脉滴注;第1天~第3天,21天重复用顺铂30mg/m²溶于0.9%的250mL生理盐水中静脉滴注;GT方案组患者有35例,吉西他滨的使用方法与GP方案组相同,第2天,21天重复用紫杉醇135mg/m²溶于0.9%的500mL生理盐水中静脉滴注。对化疗时产生的不良反应进行对症处理。

1.3 疗效评价

参照WHO在1981年制定的评价标准分为完全缓解、部分缓解、无变化和进展,分别用CR、PR、NC、PD表示。毒性作用分为无(0)、轻度(I)、中度(II)、重度(III)、威胁生命(IV)五个等级。化疗有效率用(CR+PR)/病例总数表示,疾病控制率用(CR+PR+NC)/病例总数表示。

1.4 统计学方法

采用SPSS11.0统计学软件进行统计,疗效和不良反应应用卡方检验,P<0.05为差异有统计学意义。

2 结果

2.1 化疗效果

GP方案组30例患者中CR有13.33%(4/30)、PR有33.33%(10/30)、NC有23.33%(7/30)、PD有30%(9/30),总有效率为46.67%,疾病控制率为70%。完全缓解的病例中淋巴结转移的有2例,胸壁转移的有1例,肺转移的也有1例。而GT方案组35例患者中,CR有11.43%(4/35)、PR有31.43%(11/35)、NC有25.71%(9/35)、PD有31.43%(11/35),总有效率为42.86%,疾病控制率为68.57%。其中淋巴结转移的有2例,胸壁转移和肝转移各1例。两组化疗效果比较差异无统计学意义($\chi^2=0.095$,P=0.758),两组疾病控制比较差异无统计学意义($\chi^2=0.016$,P=0.901),见表2。

表2 两组的化疗效果比较

Table 2 Comparison of the effect of chemotherapy between the two groups

组别 Groups	病例数 Cases	CR	PR	NC	PD	化疗有效率(%) Efficiency of chemotherapy(%)	疾病控制率(%) Disease control rate(%)
GP 方案组 GP regimen group	30	4	10	7	9	46.67	70.00
GT 方案组 GT regimen group	35	4	11	9	11	42.86	68.57

2.2 不良反应

患者在进行化疗后都会发生一些不良反应,如脱发、胃肠道反应、骨髓移植等,GP方案和GT方案执行后不良反应大多数是I度和II度。GP方案组发生III~IV度中发生白细胞减少的概率为13.33%,血小板减少发生的概率为6.67%,贫血发生

率为13.33%,脱发发生率为10%,恶心呕吐发生率为23.33%;GT方案组发生III~IV度中发生白细胞减少的概率为14.29%,血小板减少发生的概率为11.43%,贫血发生率为17.14%,脱发发生率为62.86%,恶心呕吐发生率为17.14%。经统计学分析,两组之间脱发的发生率差异有统计学意义(P<0.001)GT组明

表 3 两组的不良反应比较[n(%)]
Table 3 Comparison of the adverse reaction between two groups[n(%)]

组别 Groups	例数 Cases	白细胞减少 Leukocyte reduction	血小板减少 Blood platelet reduction	贫血 Anemia	脱发 Alopecia	恶心呕吐 Nausea and vomiting
GP 方案组 GP regimen group	30	4(13.33)	2(6.67)	4(13.33)	3(10.00)	7(23.33)
GT 方案组 GP regimen group	35	5(14.29)	3(8.57)	6(17.14)	22(62.86)	6(17.14)
X ²		0.012	0.083	0.180	19.068	0.387
P		0.912	0.774	0.671	<0.001	0.534

显高于 GP 组, 其他不良反应在两组之间差异无统计学意义 ($P>0.05$) 见表 3。

3 讨论

目前, 对乳腺癌的初次治疗大多是采用蒽环类药物或者紫杉类药物, 在临幊上应用广泛且取得了良好的治疗效果^[9-10]。但是对于复发转移性的乳腺癌采用何种治疗方案由于各种药物都未有达到较好的疗效在临幊一直未有统一意见^[11-12]。

吉西他滨是一种作用于细胞周期的代谢类药物, 主要作用于 S 期细胞, 即处于 DNA 合成器的肿瘤细胞^[13], 它可以通过核苷酸激酶的作用, 抑制 DNA 合成、脱氧胞嘧啶脱氨酶, 同时减少细胞内代谢物的降解^[14,15]。在采用吉西他滨的情况下, 可以有效的阻止 G1 期向 S 期进展, 这已经在胰腺癌、非小细胞型肺癌中得到了验证^[16]。近年来, 逐渐广泛应用于乳腺癌。

顺铂作用的靶点是 DNA, 其可以与 DNA 之间形成链间和链内的交链, 干扰 DNA 复制以及与核蛋白、胞浆蛋白的结合^[17]。已证实对乳腺癌、肺癌的多种肿瘤有效果^[18]。紫杉醇是植物中的一种代谢产物, 其可以结合到聚合的微管上, 而不与聚合的微管蛋白二聚体反应, 从而干扰细胞的各种功能, 阻断细胞的正常有丝分裂, 在卵巢癌、乳腺癌、肺癌等也有效果^[19-20]。

本研究选用吉西他滨与顺铂联合或者吉西他滨与紫杉醇联合治疗复发转移性乳腺癌并探讨其临床疗效, 发现两组化疗效果比较差异无统计学意义 ($P>0.05$)。两组化疗方案的不良反应大多数都是 I 度到 II 度, 在脱发、胃肠道反应、骨髓移植等不良反应中, 脱发的发生率差异有统计学意义 ($P<0.001$), GT 组显著高于 GP 组, 其他不良反应在两组之间差异无统计学意义 ($P>0.05$)。大多数的患者虽出现不同程度的恶心呕吐、厌食、贫血等不良反应, 但是在对症处理后, 均能继续进行化疗, 未发生出现严重不良反应而终止治疗的患者。

通过本研究的比较和分析, 我们发现选用吉西他滨与顺铂联合或者吉西他滨与紫杉醇联合治疗复发转移性乳腺癌均可以产生确定的疗效, 主要的不良反应为胃肠道反应、血液学毒性和脱发等, 但是只要进行对症处理, 患者均能有效的完成化疗方案, 采用这两种化疗方案治疗复发转移性乳腺癌可根据不同的患者进行选择, 是一种较好的化疗方案。

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(上接第 926 页)

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