doi: 10.13241/j.cnki.pmb.2015.02.013

紫杉醇、长春瑞滨联合顺铂方案治疗晚期乳腺癌的临床疗效

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摘要 目的：探讨紫杉醇（PTX）、长春瑞滨（NVB）两药与顺铂（DDP）联用方案对晚期乳腺癌的临床疗效及副反应。**方法：**将 2009 年 2 月至 2014 年 2 月于我院就诊的 60 例晚期乳腺癌患者随机分为 TP 方案和 NP 方案两组，每组 30 例。TP 方案组：顺铂 25 mg/m^2，d1~d3，紫杉醇 175 mg/m^2，d1；NP 方案组：顺铂 25 mg/m^2，d1~d3，长春瑞滨 25 mg/m^2，d1 和 d8。比较两组患者的临床有效率并记录相关不良反应。**结果：**TP 方案有效率 56.7%(17/30)，中位缓解期 7.5 个月。NP 方案有效率 53.3% (14/30)，中位缓解期 7.7 个月。组间疗效及缓解期差异无统计学意义（P>0.05）。TP 与 NP 方案组出现血小板减少、白细胞减少、贫血、恶心呕吐的发生率分别为 26.7%、76.7%、56.7%、43.3%和 26.7%、76.7%、56.7%、43.3%，两方案血液毒性差异无统计学意义（P>0.05）。静脉炎及关节肌肉反应的发生率分别为 30.0%、13.3%和 16.7%53.3%，差异有统计学意义（P<0.05）。**结论：**紫杉醇、长春瑞滨与顺铂联用治疗晚期乳腺癌疗效相当，不良反应可耐受，都可做为晚期乳腺癌治疗的一线用药方案。

关键词：紫杉醇；长春瑞滨；顺铂；晚期乳腺癌

中图分类号：R737.9 **文献标识码：**A **文章编号：**1673-6273(2015)02-251-03

The Clinical Effect of Paclitaxel or Vinorelbine Combined with Cisplatin in the Treatment of Advanced Breast Cancer

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ABSTRACT Objective: To study the efficacy and toxicities of paclitaxel (PTX) and vinorelbine (NVB) combined with cisplatin (DDP) in the treatment of advanced breast cancer. **Methods:** The 60 cases of patients with advanced breast cancer in our hospital from February 2009 to February 2014 were randomly divided into TP and NP group with 30 cases in each group. The patients in the TP therapy group received PTX plus DDP (PTX 175 mg/m^2, d1; DDP25 mg/m^2, d1~d3)for treatment; and the patients in the NP therapy group received the NVB plus DDP (NVB 25 mg/m^2, d1, d8, DDP 25 mg/m^2, d1~d3). The clinical effects of two groups were compared and the related adverse reactions were recorded. **Results:** In NP group, effective rate was 53.3% (14/30), and in TP group, the effective rate was 56.7%(17/30). The median response duration of NP and TP groups was 7.7 and 7.5 months respectively. The efficacy and median response duration were not significantly different between the two groups (P>0.05). The incidence rate of leucocyte reducing, plaque decreasing, vomiting and anemia in TP group and NP group were 26.7%, 76.7%, 56.7%, 43.3% and 26.7%, 76.7%, 56.7%, 43.3% respectively, there was no statistically significant difference in hematological toxicity between the two regimen groups (P>0.05). The incidence rates of phlebitis and arthritis were 30.0%, 13.3% and 16.7% , 53.3% ,with no difference between the two groups(P<0.05). **Conclusion:** TP and NP therapies for advanced breast cancer have similar efficacies and fewer adverse reactions, thus can be used as first-line treatment methods for advanced breast cancer.

Key words: Paclitaxel; Vinorelbine; Cisplatin; Advanced; Breast cancer

Chinese Library Classification(CLC): R737.9 Document code: A

Article ID:1673-6273(2015)02-251-03

前言

乳腺癌的发病率日渐提高，已成为 45~60 年龄段中年女性最常见的恶性肿瘤之一，具有多途径转移和易复发的特点[1,2]。在临床治疗中多选择手术和化疗，而顺铂则是晚期乳腺癌常选用的一线治疗方案[3-5]。随着医疗手段不断进展，临床治疗中开始将各种化疗药物联用来治疗肿瘤且取得了较好的效果[6]。本研究中选择 2009 年 2 月至 2014 年 2 月于我院就诊的 60 例晚期乳腺癌患者为研究对象，观察紫杉醇、长春瑞滨与顺铂联用对晚期乳腺癌的临床疗效及副反应，结果报告如下。

1 资料与方法

1.1 一般资料

选择 2009 年 2 月至 2014 年 2 月于我院就诊的 60 例 IV

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（收稿日期：2014-06-19 接受日期：2014-07-16）

期乳腺癌患者为研究对象,均经病理学确诊,为转移乳腺癌或术后复发患者。入录患者在一月内未进行放化疗,且心电检查、肝肾功能和血常规增均正常。卡氏(Kamofsky)评分≧70,有可测量的肿瘤观察指标,且预计生存期 >3 个月,所有患者均签署知情同意书。60 例患者随机分为 TP 方案和 NP 方案两组,每组 30 例。TP 方案组患者年龄 28~65 岁,平均年龄(45.4± 5.1)岁,绝经前 19 例,绝经后 11 例,单部位转移 15 例,多部位转移 15 例;NP 方案组患者年龄 27~66 岁,平均年龄(43.8± 3.7)岁,绝经前 17 例,绝经后 13 例,单部位转移 14 例,多部位转移 16 例。两组患者年龄、病程、转移病灶数、例假状况等资料差异无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

TP 方案组患者:紫杉醇 175 mg/m^2 加入 500 mL 0.9%氯化钠静脉滴注 3 h,d1;顺铂 25 mg/m^2 静脉滴注,d1~d3。用紫杉醇前 6 h 与 12 h 前各服 10 mg 地塞米松预防过敏反应。给药前半小时肌内注射 50 mg 苯海拉明,静脉滴 0.4 g 西咪替丁。NP 方案组患者:25 mg/m^2 长春瑞滨加入 100 mL 生理盐水, 静脉滴注,d1 和 d8,其后使用 5mg 地塞米松加入 100 mL 生理盐水冲洗血管防止长春瑞滨对静脉的刺激,顺铂用法同 TP 方案组。化疗化程中出现胃肠道症状静脉滴注昂丹司琼止吐。两种方案 21 天为一周期,每例患者进行 2~6 个周期。

1.3 疗效判定与观察指标

依据 WHO 标准[7],将治疗效果分为如下四个:进展(PD)、稳定(SD)、部分缓解(PR)和完全缓解(CR)。按照 WHO 抗癌药物亚急性和急性毒性表现分级标准可将不良反应分为 0 级(无)、I 级(轻度)、II 级(中度)、III 级(重度)、IV 级(危及生命)[8]。

1.4 统计学处理

运用 SPSS18.0 统计学软件进行分析, 数据采用 X^2 检验,P<0.05,差异有统计学意义。

2 结果

2.1 近期疗效

TP 方案组有效率为 56.7%,中位缓解期 7.5 个月;NP 方案组有效率为 53.3%,中位缓解期 7.7 个月。两组有效率比较,X^2 = 0.219,P=0.640 > 0. 05,差异无统计学意义,结果见表 1。

表 1 两种方案疗效比较

Table 1 Coparison of clinical effect between the two groups

治疗方案 Therapeutic regimen	n	疗效 Effect				有效率(%) Effective rate(%)	X^2	P
		PD	SD	PR	CR			
TP	30	7	10	10	3	56.7%	0.219	0.640
NP	30	5	9	12	4	53.3%		

2.2 不良反应比较

两种治疗方案的主要不良反应都为血液毒性,其次为关节肌肉疼痛、静脉炎和恶心呕吐,结果显示,两组方案血小板量、白细胞量的变化、贫血和恶心呕吐的发生率比较差异均无统计学意义(P>0.05),而静脉炎及关节肌肉反应的发生率差异有统计学意义(P<0.05),见表 2。

表 2 不良反应结果比较

Table 2 Comparison of adverse reactions

不良反应 Adverse reaction	0		I		II		III		IV		发生率(%) Incidence rate (%)		X^2	P
	NP	TP	NP	TP	NP	TP	NP	TP	NP	TP	NP	TP		
白细胞减少 Plaque decreasing	9	7	7	3	4	3	8	13	2	4	70.0	76.7	1.152	0.281
血小板减少 Leucocyte reducing	21	22	5	2	2	3	2	0	0	3	30.0	26.7	0.275	0.595
恶心呕吐 Vomiting	17	17	5	7	4	5	4	1	0	0	43.3	43.3	0.001	1.000
贫血 Anemia	14	13	3	8	4	4	6	3	3	2	53.3	56.7	0.239	0.328
肌肉关节疼痛 Muscle and joint pain	26	14	1	14	2	1	1	1	0	0	13.3	53.3	36.047	0.000
静脉炎 Phlebitis	21	25	4	1	3	1	1	2	1	1	30.0	16.7	4.949	0.032

3 讨论

乳腺癌在临床治疗中多选择手术和化疗,而顺铂则是其常选用的一线治疗方案。近年来随着紫杉醇、长春瑞滨等新型药物的出现,联合化疗已成为晚期乳腺癌的重要治疗方法[9,10]。国内外多篇文献显示即使在常用的蒽环类药物失败的情况下它们在晚期乳腺癌的治疗中也能有较高的活性,且有更长的缓解期及更高的有效率[11-13]。

顺铂是一种类似双功能烷化剂的重金属络合物,顺铂细胞敏感性较高,高浓度时可抑制 RNA 和蛋白质合成,抑制 DNA 的复制过程。顺铂可通过扩散作用通过细胞膜, 主要作用于 DNA 的嘧啶和嘌呤碱基。顺铂有细胞毒性,属于非特异性细胞周期药物,可抑制癌细胞的 DNA 复制过程,并损伤其细胞膜上结构,有较强的广谱抗癌作用。长春瑞滨是新型的植物性抗肿瘤药,它特异性的作用于肿瘤细胞的有丝分裂期,对微管蛋白有很高的亲和力,它可抑制微管蛋白合成微管的能力,解聚微管,抑制细胞的有丝分裂及增殖,从而发挥抗肿瘤的作用[14]。在诸多相关文献中显示, 长春瑞滨对肿瘤有很好的治疗效果,对转移性乳腺癌单药一线治疗时有效率即可达到 40%~60%,且毒副作用可耐受[15-17]。当其与顺铂合用时可产生协同作用治疗乳腺癌,且与其它化疗药无交叉耐受性,在相关文献中报道当二者联合治疗晚期乳腺癌时有效率可达 50%以上[18,19]。在本研究中长春瑞滨与顺铂联用治疗晚期乳腺癌有效率可达 55%,与其它报道结果基本一致[20]。紫杉醇属于植物类抗肿瘤药,可特异性的结合于癌细胞小管的 β 位,促进微管聚合,从而抑制其正常功能,对细胞有丝分裂进行干扰并诱导细胞凋亡。临床调查发现紫杉醇对转移性乳腺癌单药一线治疗时有效率可达 32%~60%, 当与顺铂合用时不良反应重叠较少且无交叉耐药性。体外实验结果表明,使用紫杉醇后再用顺铂,两者具有协同或相加作用。在本研究中 TP 方案和 NP 方案在治疗晚期乳腺癌中有效率分别为 56.7%和 53.3%,二者疗效相当,无显著性差异(P>0.05)。两种方案主要不良反应都为血液毒性,其次为关节肌肉疼痛、静脉炎和恶心呕吐,两组均未发生治疗相关性死亡。本研究结果显示,两组方案血小板量、白细胞量的变化、贫血和恶心呕吐的发生率比较差异均无统计学意义(P>0.05),而静脉炎及关节肌肉反应的发生率差异有统计学意义(P<0.05),但程度轻微,在调查中发现采用深静脉置管进行滴注的患者静脉炎发生率较低,提示临床用药过程中采用深静脉置管进行滴注可降低相关不良反应。

综上所述,紫杉醇或长春瑞滨与顺铂联用治疗晚期乳腺癌疗效相当,不良反应可耐受,都可做为对蒽坏类药物无效的晚期乳腺癌治疗的一线用药方案。

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疗效好,患者的不良反应小且耐受性好等特点,临床有重要参考价值。

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