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多西紫杉醇联合卡铂治疗老年子宫内膜癌的疗效及安全性

张卫霞 闫飞艳 白小英 杨 婷 陈 娜

(西安医学院第二附属医院妇科 陕西 西安 710038)

摘要 目的:探讨多西紫杉醇与卡铂联合化疗在老年子宫内膜癌患者中的疗效及安全性。**方法:**选择2010年1月至2016年1月我院收治的子宫内膜癌患者78例作为研究对象,其中年龄<60岁的患者42例纳入非老年组,年龄≥60岁的患者36例纳入老年组,均给予多西紫杉醇与卡铂联合化疗。对两组患者一般情况、化疗实施情况、临床疗效以及毒副反应进行观察与比较。**结果:**两组患者组织学分型有明显差异($P<0.05$),其他一般资料无显著差异($P>0.05$)。老年组患者采用低剂量完成化疗的比例明显高于非老年组,差异有统计学意义($P<0.05$),化疗周期及中断率无显著差异($P>0.05$)。两组患者临床疗效、血液系统毒副反应及消化系统毒副反应发生率均差异不显著($P>0.05$)。**结论:**多西紫杉醇与卡铂联合化疗在老年子宫内膜癌患者中治疗效果与非老年患者类似,安全性尚可,值得临床推广应用。

关键词:子宫内膜癌;老年患者;多西紫杉醇;卡铂

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Clinical Effect and Safety of Docetaxel Combined with Carboplatin in Treatment of Elderly Patients with Endometrial Cancer

ZHANG Wei-xia, YAN Fei-yan, BAI Xiao-ying, YANG Ting, CHEN Na

(Gynecology Department, The Second Affiliated Hospital of Xi'an Medical University, Xi'an, Shaanxi, 710038, China)

ABSTRACT Objective: To explore the clinical effect and safety of docetaxel combined carboplatin in treatment of elderly patients with endometrial cancer. **Methods:** 78 patients with endometrial cancer accepted in our hospital from January 2010 to January 2016 were selected. 42 patients with age <60 were admitted into non-elderly group, and 36 patients with age >60 were considered as elderly group. All the patients were given docetaxel combined carboplatin. Then the general situation, chemotherapy implementation, clinical effect and toxicity reactions of two groups were observed and compared. **Results:** The histologic classification of two groups had significantly difference ($P<0.05$), but other general situations had no statistical difference ($P>0.05$). The patients using low dose in chemotherapy of elderly group were much more than that of non-elderly group with statistically significance ($P<0.05$), but the period and interruption rate of two groups had no statistical difference ($P>0.05$). The clinical effect and the rate of toxicity reactions of two groups had no statistical difference ($P>0.05$). **Conclusions:** Using docetaxel combined with carboplatin for elderly patients with endometrial cancer is as effective as non-elderly patients with good safety, worth of clinical applications.

Key words: Endometrial cancer; Elderly; Docetaxel; Carboplatin

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前言

子宫内膜癌是一组发生于子宫内膜的上皮性恶性肿瘤,是女性最为常见的生殖系统恶性肿瘤之一,也是导致死亡的第三位妇科恶性肿瘤^[1]。子宫内膜癌好发于围绝经期和绝经后女性,且随着人口老龄化水平的不断发展,老年子宫内膜癌所占的比例也呈逐渐升高趋势^[2]。有研究报道显示,约有半数以上的子宫内膜癌患者诊断时年龄≥60岁^[3]。目前,针对老年子宫内膜癌患者的治疗多以放化疗为主,而联合化疗可最大化的提高药物作用能力,从而使患者获得更加满意的临床疗效^[4]。但是,老年患者往往身体状况较差,对于化疗耐受程度较低,易发生毒副

反应^[5],因此联合化疗的安全性仍然有待考察。本研究近年来使用多西紫杉醇与卡铂联合治疗老年子宫内膜癌,取得了良好的临床效果,并且安全性尚可,患者耐受程度较好,故特此报道。

1 资料与方法

1.1 一般资料

78例2010年1月至2016年1月间就诊的子宫内膜癌患者为本回顾性分析的研究对象,纳入及排除标准如下:①所有患者均经明确的影像学或病理学诊断为子宫内膜癌;②排除合并其他系统严重疾病,如心功能不全或肝肾功能障碍等;③排除有相关化疗药物使用禁忌症。将78例患者按照年龄大小将其进行分组,其中年龄<60岁的患者42例纳入非老年组,年龄≥60岁的患者36例纳入老年组。非老年组患者平均年龄(42.7±6.5)岁,老年组患者平均年龄(63.9±5.2)岁。

作者简介:张卫霞(1982-),女,硕士,主治医师,主要研究方向:妇科肿瘤,电话:13572888401,

E-mail: zhangweixia_1982@medicine360.net

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1.2 治疗方法

两组患者均使用多西紫杉醇与卡铂联合化疗,具体用药方案如下:多西他赛注射液(商品名:泰素帝;生产厂家:英国 Aventis Pharma S.A.;批准文号:H20090494)75 mg/m²于 d1 静脉滴注 3 h;卡铂注射液(商品名:伯尔定;生产厂家:Corden Pharma Latina S.P.A.;批准文号:H20110231)300 mg/m²于 d2 静脉滴注。21 d 为 1 个周期。常规治疗 3 周期,对于尚未达到治疗标准的患者继续治疗。

1.3 评价指标

对两组患者一般情况、化疗实施情况、临床疗效以及毒副反应进行观察与比较,具体指标如下:① 一般情况:包括病理分期、病理分级、组织学类型以及体力状况 ECOG 评分^[6];② 化疗实施情况:记录两组患者实施周期以及剂量减低、治疗中断的例数及原因;③ 临床疗效:按照 RECIST 疗效评价标准^[7],将疗效划分为完全缓解(CR)、部分缓解(PR)、疾病稳定(SD)以及疾病进展(PD),中断治疗的患者在中断治疗后评价,未中

断治疗的患者在三个疗程结束后进行评价;④ 毒副反应:记录两组患者治疗结束时血液系统及消化系统毒副反应发生例数,评级参考 WHO 制定的化疗药物毒副反应评价标准^[8]。

1.4 统计学方法

采用 SPSS 19.0 统计学软件进行数据处理,计数资料以率的形式表示,检验方法选择卡方检验或秩和检验。假设检验标准为 $\alpha=0.05$ 。

2 结果

2.1 两组患者一般情况比较

对两组患者一般情况进行比较,结果显示,老年组患者病理分期及病理分级均略高于非老年组患者,但差异无统计学意义($P>0.05$)。非老年组以内膜样癌最为多见,所占比例明显高于老年组,差异有统计学意义($P<0.05$)。两组患者 ECOG 评分无明显差别。见表 1。

表 1 两组患者一般情况比较 [n(%)]

Table 1 Comparison of general situations of two groups [n(%)]

Items	Non-elderly group(n=42)	Elderly group(n=36)	χ^2	P
Pathology Stage			3.302	0.069
I ~ II	25(59.52)	14(38.89)		
III~IV	17(40.48)	22(61.11)		
Pathology Grade			5.933	0.051
1	22(52.38)	11(30.56)		
2	8(19.05)	5(13.89)		
3	12(28.57)	20(55.56)		
Histologic classification			8.268	0.041
Endometrioid carcinoma	37(88.10)	22(61.11)		
Mucinous carcinoma	1(2.38)	5(13.89)		
Serous carcinoma	2(4.76)	6(16.67)		
Undifferentiated carcinoma	2(4.76)	3(8.33)		
ECOG score			3.655	0.161
0	40(95.24)	30(83.33)		
1	2(4.76)	4(11.11)		
2	0(0.00)	2(5.56)		

2.2 两组患者化疗实施情况比较

对两组患者化疗实施情况进行比较,结果显示,非老年组实施周期短于老年组,但不具有统计学差异($P>0.05$)。老年组 44.44 %患者减低剂量,远高于非老年组 21.43 %,差异有统计学意义($P<0.05$)。减低剂量的原因包括血液系统毒性以及非血液系统毒性。老年组 33.33 %患者中断治疗,其中 6 名患者于治疗 2 疗程后中断,6 名于治疗 3 疗程后中断;非老年组 19.05 %患者中断治疗,其中 3 名于治疗 2 疗程后中断,5 名于治疗 3 疗程后中断。两组患者治疗中断率及治疗中断时间差异不显著($P>0.05$)。治疗中断的原因包括毒性反应、疾病进展以及患者主动退出。见表 2。

2.3 两组患者临床疗效比较

治疗结束时对两组患者疗效进行比较,结果显示,两组患

者临床疗效无显著差异($P>0.05$)。见表 3。

2.4 两组患者血液系统毒副反应发生情况比较

两组患者血液系统毒副反应发生情况及严重程度均无显著差异($P>0.05$)。见表 4。

2.5 两组患者消化系统毒副反应发生情况比较

两组患者消化系统毒副反应发生情况及严重程度均无显著差异($P>0.05$)。见表 5。

3 讨论

化疗一直是治疗子宫内膜癌的常见方法,然而化疗药物种类及联合化疗方案均较多,选择合适的化疗方案一直是临床医师不断探索的问题。近年来,多西紫杉醇与卡铂联合化疗已被较多应用于非小细胞肺癌、乳腺癌等疾病的治疗当中,并取得

了良好的临床疗效,然而其治疗子宫内膜癌的研究在国内尚不多见^[9-11]。Geller 等研究结果显示,卡铂与多西紫杉醇联合化疗治疗晚期或复发子宫内膜癌可有效提高患者生存率^[12];Nor-

mura 等的研究也同样证实了这一点^[13]。故本研究选择使用卡铂与多西紫杉醇联合化疗对老年子宫内膜癌患者进行治疗。

表 2 两组患者化疗实施情况比较 [n(%)]

Table 2 Comparison of chemotherapy implementation of two groups [n(%)]

Items	Non-elderly group(n=42)	Elderly group(n=36)	Z/x ²	P
Implementation period			4.161	0.125
1~3	17(40.48)	8(22.22)		
4~6	21(50.00)	20(55.56)		
>6	4(9.52)	8(22.22)		
Dose decreasing	9(21.43)	16(44.44)	4.715	0.030
Reasons				
Blood system toxicity reactions	4(9.52)	9(25.00)		
Non-blood system toxicity reactions	5(11.90)	7(19.44)		
Treatment interruption	8(19.05)	12(33.33)	2.075	0.150
Reasons				
Toxicity reactions	6(14.29)	7(19.44)		
Disease progression	2(4.76)	4(11.11)		
Patients quit	0(0.00)	1(2.78)		

表 3 两组患者临床疗效比较 [n(%)]

Table 3 Comparison of clinical effect of two groups [n(%)]

Groups	n	CR	PR	SD	PD
Non-elderly group	42	7(16.67)	14(33.33)	12(28.57)	9(21.43)
Elderly group	36	5(13.89)	11(30.56)	10(27.78)	10(27.78)
Z			0.630		
P			0.529		

表 4 两组患者血液系统毒副反应发生情况比较 [n(%)]

Table 4 Comparison of blood system toxicity reactions of two groups [n(%)]

Items	Non-elderly group(n=42)	Elderly group(n=36)	x ²	P
Neutropenia	33(78.57)	31(86.11)	0.748	0.387
Grade I~II	21(50.00)	20(55.56)		
Grade III~IV	12(28.57)	11(30.56)		
Leukopenia	34(80.95)	30(83.33)	0.075	0.785
Grade I~II	18(42.86)	16(44.44)		
Grade III~IV	16(38.10)	14(38.89)		
Anaemia	36(85.71)	30(83.33)	0.084	0.771
Grade I~II	23(54.76)	18(50.00)		
Grade III~IV	13(30.95)	12(33.33)		
Thrombocytopenia	28(66.67)	25(69.44)	0.069	0.793
Grade I~II	26(61.90)	21(58.33)		
Grade III~IV	2(4.76)	4(11.11)		

在研究之初,我们对老年患者及非老年患者的一般资料进行了考察,结果显示,除组织学类型外,两组患者一般资料均无明显差异。这可能是由于老年患者身体状况明显较差,故可见恶性程度较高的病理类型,与文献报道相似^[14]。在对化疗实施情况进行的考察当中,我们发现部分患者由于化疗毒副反应无

法按照原定计划进行治疗,而进行了剂量调整^[15,16]。此种剂量调整发生率在老年患者中显著高于非老年患者,这可能与老年患者的身体耐受性较差有关^[17]。此外,我们还观察到部分患者出现治疗中断现象,对于毒副反应造成的中断,我们先进行了相关对症治疗,缓解后再按照原定方案进行治疗^[18,19];对于疾病进

展或患者要求退出造成的中断,我们根据患者自身情况换用其他方案进行治疗^[20]。在治疗结束时,我们对两组患者疗效及毒副反应进行了评价,结果显示,两组患者无显著差别。提示多西

紫杉醇与卡铂联合化疗对于老年子宫内膜癌患者治疗效果与非老年患者类似。

表 5 两组患者消化系统毒副反应发生情况比较 [n(%)]
Table 5 Comparison of digestive system toxicity reactions of two groups [n(%)]

Items	Non-elderly group(n=42)	Elderly group(n=36)	χ^2	P
Nausea	19(45.24)	21(58.33)	1.331	0.249
Grade I~II	16(38.10)	20(55.56)		
Grade III~IV	3(7.14)	1(2.78)		
Vomit	8(19.05)	7(19.44)	0.002	0.965
Grade I~II	8(19.05)	7(19.44)		
Grade III~IV	0(0.00)	0(0.00)		
Diarrhea	6(14.29)	9(25.00)	1.433	0.231
Grade I~II	6(14.29)	7(19.44)		
Grade III~IV	0(0.00)	2(5.56)		
Liver function damage	4(9.52)	3(8.33)	0.034	0.854
Grade I~II	4(9.52)	3(8.33)		
Grade III~IV	0(0.00)	0(0.00)		

随着癌症相关研究的不断深入,联合化疗方案已被人们广泛认可和接受。与其他研究不同的是,我们并未对联合化疗与单药化疗方案的优势与劣势进行比较,而是对特定人群 -- 老年子宫内膜癌患者进行了观察与分析,并得到了较为满意的结果。然而本研究尚存在例数过少、对照组设计不够严密等问题,这也提示我们将今后工作的重点放在严密设计的大样本量多中心随机对照试验当中。

综上所述,多西紫杉醇与卡铂联合化疗在老年子宫内膜癌患者中治疗效果与非老年患者类似,安全性尚可,值得临床推广应用。

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