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艾迪注射液联合化疗对卵巢癌患者血清 HE4, CA125, CA19-9, AFP, CEA 水平及 T 细胞亚群的影响 *

崔艳艳¹ 綦会霞¹ 常桂花¹ 房芹¹ 王亚丽¹ 王玉敏¹ 伍婕²

(1 赤峰学院附属医院 肿瘤内科 内蒙古 赤峰 024000; 2 内蒙古赤峰市医院 皮肤性病科 内蒙古 赤峰 024000)

摘要 目的:探讨艾迪注射液联合化疗对卵巢癌患者血清人附睾蛋白 4(HE4)、糖类抗原 125(CA125)、糖类抗原 19-9(CA19-9)、甲胎蛋白(AFP)、癌胚抗原(CEA)及 T 细胞亚群的影响。**方法:**选取我院 2014 年 8 月至 2016 年 2 月收治的 78 例卵巢癌患者,按照随机数表法将其分为观察组(n=39)和对照组(n=39),对照组患者给予化疗,观察组患者给予艾迪注射液联合化疗,比较两组患者的临床疗效、治疗前后血清 HE4、CA125、CA19-9、AFP、CEA 水平及 T 细胞亚群的变化。**结果:**治疗后,观察组的总有效率(94.87%)显著高于对照组(76.92%) (P<0.05)。治疗后,两组患者血清 HE4、CA125、CA19-9、AFP、CEA 水平均较治疗前明显下降,且观察组显著低于对照组 (P<0.05)。治疗后,两组患者 CD3⁺、CD4⁺、CD8⁺较治疗前均显著降低,且观察组患者 CD3⁺、CD4⁺、CD8⁺低于对照组 (P<0.05)。**结论:**艾迪注射液联合化疗对卵巢癌治疗效果显著,能有效降低血清 HE4、CA125、CA19-9、AFP、CEA 水平并改善患者免疫功能。

关键词:艾迪注射液;卵巢癌;人附睾蛋白 4;糖类抗原 125;糖类抗原 19-9;甲胎蛋白;癌胚抗原;T 细胞亚群

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Effect of Aidi Injection Combined with Chemotherapy on Serum Levels of HE4, CA125, CA19-9, AFP and CEA and T Cell Subsets of Patients with Ovarian Cancer*

CUI Yan-yan¹, QI Hui-xia¹, CHANG Gui-hua¹, FANG Qin¹, WANG Ya-li¹, WANG Yu-min¹, WU Jie²

(1 Department of oncology, Hospital Affiliated to Chifeng College, Chifeng, Inner Mongolia, 024000, China;

2 Department of Dermatology of Chifeng Hospital, Chifeng, Inner Mongolia, 024000, China)

ABSTRACT Objective: To study the effect of Aidi injection combined with chemotherapy on the serum levels of HE4, CA125, CA19-9, AFP, CEA and T cell subsets in patients with ovarian cancer. **Methods:** 78 cases with ovarian cancer admitted in our hospital from August 2014 to February 2016 were selected and randomly divided into the observation group (n=39) and the control group (n=39). The patients in the control group were treated with chemotherapy, and the patients in the observation group were treated with aidi injection combined with chemotherapy. Then the clinical effect, the serum levels of HE4, CA125, CA19-9, AFP, CEA and T cell subsets between the two groups were observed and compared before and after the treatment. **Results:** The total effective rate in the observation group was 94.87%, which was higher than that of the control group (P<0.05). The serum levels of HE4, CA125 and CA19-9 in the two groups after treatment were lower than before, and the observation group was lower than that of the control group (P<0.05). The serum levels of AFP and CEA of patients in the two groups after treatment were significantly lower than before, and the observation group was lower than that of the control group (P<0.05). The ratio of CD3⁺, CD4⁺ and CD8⁺ in the two groups after treatment were significantly lower than before, and the observation group was significantly lower than that of the control group (P<0.05). **Conclusion:** Aidi injection combined with chemotherapy has remarkable clinical effects on the treatment of ovarian cancer, which can reduce the serum levels of CA125, CA19-9, AFP, CEA and T cell subsets, and improve the immune functions of patients.

Key words: Aidi injection; Chemotherapy; Ovarian cancer; HE4; CA125; CA19-9; AFP; CEA; T cell subsets

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前言

近年来,我国卵巢癌的发病率逐年升高,且多数患者在初诊时已属肿瘤晚期,失去了手术切除的机会,生存率较低^[1]。化

疗是目前临床上应用较广的治疗方案,但在化疗过程中会出现脱发、恶心呕吐等不良反应。此外,还有一些化疗药物具有极强的消化毒性,严重影响患者治疗效果和预后^[2,3]。因此,寻找一种毒性小、不良反应少的化疗药物已成为医学界的一大重点和难

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作者简介:崔艳艳(1974-),女,硕士,副主任医师,研究方向:消化系统肿瘤化疗及靶向治疗,电话:17704768616

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题。艾迪注射液是由多种中药提炼而成,具有抗癌细胞的作用,这为研究治疗卵巢癌提供了新方向^[4]。同时,还有研究表明艾迪注射液中斑蝥素在抑制肿瘤细胞的同时还能避免降低周围白细胞计数,这在抗癌药物中极少见^[5]。因此,本研究采用艾迪注射液联合化疗治疗卵巢癌患者,探讨联合治疗对患者血清HE4、CA125、CA19-9、AFP、CEA水平及T细胞亚群的影响,现进行如下报道。

1 材料与方法

1.1 临床资料

选取2014年8月至2016年2月在我院治疗的卵巢癌患者共计78例,随机分为观察组和对照组,每组各39例。其中,观察组年龄33~63岁,平均年龄(57.41±7.03)岁;对照组年龄35~61岁,平均年龄(57.37±7.12)岁。纳入标准^[6]:①经确诊为卵巢癌;②年龄大于18岁;③患者属首次接受化疗。排除标准:①患者同时患有其他恶性肿瘤;②妊娠期或哺乳期妇女;③有化疗禁忌症。整个研究经患者及其家属知情同意并签署相关书面同意书,同时在我院伦理委员会批准下实施。两组患者在临床资料方面的比较差异无明显统计学意义(P>0.05),具有可比性。

1.2 治疗方法

对照组患者给予常规化疗的方法进行治疗。以静脉滴注方式给予患者紫杉醇(生产厂家:海南紫杉园制药有限公司;生产批号:20120509;规格:5 mL:30 mg)175 mg/m²加生理盐水。卡

铂注射液(生产厂家:齐鲁制药有限公司;生产批号:20100930;规格:10 mL:100 mg)75 mg/m²,分为连续三天静脉滴注。三周为一个周期,两个周期后观察疗效。观察组患者在对照组基础上联合应用艾迪注射液(生产厂商:贵州益佰制药股份有限公司;生产批号:20030913;规格:每支装10 mL)。每日静脉滴注70 mL艾迪注射液加600 mL生理盐水,周期与化疗同步。

1.3 观察指标

血清学指标检测:两组患者于治疗前后分别空腹采集静脉血,离心分离血清后备用。采用ELISA法进行HE4、CA125、CA19-9、AFP、CEA及T细胞亚群水平检测。

疗效评定标准:痊愈:肿瘤消失;显效:肿瘤体积减少1/2以上;有效:肿瘤体积减少1/4以下;无效:肿瘤体积增大或出现新病灶^[7]。有效率=(痊愈+显效+有效)/总例数×100%。

1.4 统计学处理

采用SPSS 14.5 for windows软件进行统计学处理,计量资料以均数±标准差($\bar{x} \pm s$)表示,采用t检验,计数资料以百分率表示,采用 χ^2 检验,以P<0.05时为差异具有统计学意义。

2 结果

2.1 两组患者治疗后的疗效比较

治疗后,观察组总有效率(94.87%)明显高于对照组(76.92%),差异具有统计学意义(P<0.05),见表1。

表1 两组患者治疗后疗效比较[例(%)]

Table 1 Comparison of the curative effect between two groups [n(%)]

Groups	n	Markedly	Effective	Invalid	Effective rate(%)
Observation group	39	24	13	2	94.87
Control group	39	18	12	9	76.92

2.2 两组患者治疗前后血清HE4、CA125、CA19-9水平的变化

治疗后,两组患者的血清HE4、CA125、CA19-9水平均较治疗前明显下降,差异有统计学意义(P<0.05);且观察组患者血

清HE4、CA125、CA19-9与对照组相比明显更低,差异有明显统计学意义(P<0.05),见表2。

表2 两组患者治疗前后血清HE4、CA125、CA19-9水平的变化比较

Table 2 Comparison of the serum HE4, CA125, CA19-9 levels between two groups before and after treatment($\bar{x} \pm s$)

Groups	n	Time	HE4(pmol/L)	CA125(U/mL)	CA19-9(U/mL)
Observation group	39	Before treatment	278.42±23.59	218.45±49.67	158.82±39.51
		After treatment	29.36±13.47**	18.06±9.82**	12.16±5.19**
Control group	39	Before treatment	279.16±23.11	217.14±45.32	159.08±39.11
		After treatment	75.68±14.52*	38.51±19.22*	35.47±9.84*

Note: compared with the control group, *P<0.05; compared with before treatment, **P<0.05.

2.3 两组患者治疗前后血清AFP、CEA水平的变化

治疗后,两组患者血清AFP、CEA水平均较治疗前显著降

低(P<0.05);观察组患者治疗后血清AFP、CEA水平较对照组更低(P<0.05),见表3。

表3 两组患者治疗前后血清AFP、CEA水平变化比较

Table 3 Comparison of the serum AFP, CEA levels between two groups before and after treatment($\bar{x} \pm s$, ng/mL)

Groups	n	Time	AFP	CEA
Observation group	39	Before treatment	87.49±8.06	31.30±7.53
		After treatment**	4.32±1.27	2.01±0.36**
Control group	39	Before treatment	87.56±8.25	32.72±6.94
		After treatment*	9.62±1.41	4.47±1.05*

Note: Compared with the control group, *P<0.05; Compared with before treatment, **P<0.05.

2.4 两组患者治疗前后 T 细胞亚群的变化

治疗后,两组患者 CD3⁺、CD4⁺、CD8⁺ 所占比值较治疗前均

显著降低,但观察组患者各指标均明显高于对照组(P<0.05),详见表 4。

表 4 两组患者治疗前后 T 细胞亚群变化比较

Table 4 Comparison of the T cell subset levels between two groups before and after treatment($\bar{x} \pm s, \%$)

Groups	n	Time	CD3 ⁺	CD4 ⁺	CD8 ⁺
Observation group	39	Before treatment	71.13± 8.25	39.12± 9.18	32.57± 5.32
		After treatment	54.02± 4.68* [#]	31.26± 4.83	20.16± 1.24* [#]
Control group	39	Before treatment	71.25± 8.39	40.24± 9.34	33.05± 4.83
		After treatment	36.21± 4.50*	19.06± 4.51	11.67± 1.19*

Note: Compared with the control group, [#]P<0.05; Compared with before treatment, *P<0.05.

3 讨论

卵巢癌是与子宫颈癌、子宫体癌排在前三的女性生殖器官严重疾病,严重影响女性的生活质量和生命健康^[8]。卵巢癌多发生于围绝经期的妇女群体,临床主要表现为腹胀、腹痛、不正常消瘦、月经不稳定等,目前其发病机制尚不完全明确,可能与致癌因子、免疫功能、内分泌、遗传以及饮食、生活习惯等有关^[9,10]。目前临床主要应用化疗对卵巢癌进行治疗,主要治疗药物包括铂类抗肿瘤药物和紫杉醇等^[11]。研究显示紫杉醇联合铂类抗肿瘤药物治疗虽然对肿瘤细胞有一定的抑制作用,但其对患者神经系统和消化道系统带来的毒性也不容忽视,严重影响整体治疗效果和预后情况^[12,13]。此外,化疗对正常细胞也有一定的损伤。艾迪注射液由斑蝥、黄芪、人参、刺五加等多种中药成分组成,具有消瘀散结、清热解暑等功效。药方中斑蝥不仅效果显著,且无明显的免疫抑制作用,而黄芪、人参和刺五加则可以抑制肿瘤血管生成、肿瘤细胞增殖以及诱导肿瘤细胞的凋亡,因此可用于妇科恶性肿瘤,有抗癌、增强免疫功能^[14,15]。本研究在化疗基础上联合艾迪注射液对患者进行治疗,其临床总有效率可达 94.87%,表明艾迪注射液联合化疗的疗效更高。

血清 HE4、CA125、CA19-9、AFP、CEA 及 T 细胞亚群等是临床上诊断及预后判断的卵巢癌肿瘤标志物,对其水平变化的监测可用于指导患者诊断、治疗和预后^[16]。HE4 是 Whey 酸性蛋白家族分泌蛋白的一种,其敏感性较高,对卵巢上皮细胞具有较高的特异性、敏感性和高度表达性。CA125 则在浆液性卵巢癌中具有较高的表达性,并随着肿瘤的进展逐渐升高。CA19-9 在正常人体组织中几乎不存在,但其在肿瘤组织中的含量随病程进展而上升。AFP 属于胚胎卵黄囊表达球蛋白,其水平同 CA125 一样在卵巢癌中随病情发展而逐渐升高。CEA 作为广谱非特异性肿瘤标志物,其在卵巢癌组织中也有表达^[17]。相关研究表明应用艾迪注射液联合化疗可有效降低 HE4、CA125、CA19-9 水平表达^[18]。本研究结果也表明艾迪注射液可显著降低 HE4、CA125、CA19-9 在卵巢癌中的表达,与上述研究结果一致,说明艾迪注射液联合化疗对降低 HE4、CA125、CA19-9 水平有积极影响。同时,本研究发现患者经治疗 AFP、CEA 水平均显著下降,并且经艾迪注射液联合化疗的患者 AFP、CEA 水平下降更明显,提示化疗可一定程度上减少肿瘤细胞,且联合艾迪注射液治疗的临床效果更为明显,对控制肿瘤细胞扩散具有重要意义。T 细胞亚群的变化可以检测免

疫功能在患者病情变化中的状态,辅助临床疾病的诊断^[19,20]。因此,卵巢癌患者体内 T 细胞亚群含量会增高,随着病情缓解而下降。本研究中,患者治疗后体内 CD3⁺、CD4⁺、CD8⁺ 含量均下降,但艾迪注射液联合化疗的患者优于单纯化疗者,说明联合治疗对改善卵巢癌患者免疫功能更为有效。

总之,艾迪注射液联合化疗对卵巢癌治疗效果显著,能有效降低血清 HE4、CA125、CA19-9、AFP、CEA 水平并改善患者免疫功。

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