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EMA/CO 化疗方案治疗恶性滋养细胞肿瘤的临床疗效观察 *

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摘要 目的:恶性滋养细胞肿瘤(Malignant trophoblastic tumor)是胚胎滋养细胞发生病变而产生的恶性肿瘤,严重威胁女性患者的身体健康及生活质量。本研究对 EMA/CO(etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine)化疗方案治疗恶性滋养细胞肿瘤的临床效果及毒副反应情况进行探讨,旨在为该病的临床治疗积累经验。**方法:**选取我院 2010 年 8 月 -2012 年 12 月收治的恶性滋养细胞肿瘤患者 58 例,随机分为研究组和对照组,每组各 29 例。对照组采用 5-Fu+KSM 方案进行治疗,研究组采用 EMA/CO 方案治疗。观察并比较两组患者的治疗总有效率及毒副反应的发生情况。**结果:**对照组治疗总有效率为 75.9%,研究组治疗总有效率为 79.3%,两组患者的临床疗效无显著差异(P<0.05)。研究组白细胞减少、呕吐及口腔溃疡程度均比对照组轻,差异具有统计学意义(P<0.05)。**结论:**应用 EMA/CO 化疗方案治疗恶性滋养细胞肿瘤具有积极的作用,不但可以获得较好的近期疗效,且毒副反应较轻,值得临床应用推广。

关键词:恶性滋养细胞肿瘤;EMA/CO 化疗方案;临床疗效;毒副反应

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Clinical Observation on the Efficacy of EMA/CO Regimen on the Treatment of Malignant Trophoblastic Tumor*

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ABSTRACT Objective: Malignant trophoblastic tumor is a kind of cancer that brought by the pathological changes of embryonic nourish cells which would seriously influence the health and life of female patients. This article is written to discuss the clinical effects and adverse reactions that induced by the chemotherapy of EMA/CO on the treatment of malignant trophoblastic tumor so as to accumulate the experience for clinical treatment. **Methods:** 58 cases with malignant trophoblastic tumor who were treated in our hospital from August 2010 to December 2012 were selected and randomly divided into the study group and the control group with 29 in each one. The patients in the control group were treated by 5-Fu+KSM, while the patients in the study group were given the EMA/CO. Then the rate of total efficacy and the incidence of adverse reactions of patients were observed and compared between the two groups. **Results:** The rate of total efficacy in the control group was 75.9% which was similar to the 79.3% in the study group with no significant difference(P<0.05). There were statistically significant differences about the leukopenia reduction, the vomiting and the oral cavity ulcer of patients between the two groups(P<0.05). **Conclusions:** It is indicated that the application of EMA/CO on the treatment of malignant trophoblastic tumor should be well promoted to the clinical field with the advantages of better efficacy and lighter adverse reaction.

Key words: Malignant trophoblastic tumor; EMA/CO chemotherapy; Clinical efficacy; Adverse reaction

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前言

恶性滋养细胞肿瘤是女性常见的恶性肿瘤之一,临床上主要包括侵袭性葡萄胎和绒毛膜癌,该病恶性程度较高且好发于育龄女性,对女性的身心健康造成极大的影响[1]。与传统手术治疗相比,化疗不仅能够有效杀死肿瘤细胞,而且不会破坏女性的解剖结构,因此深受育龄期女性,特别是希望保留生育功能的女性患者的青睐[3-5]。目前,临床上应用较广的化疗方案主要为 EMA/CO 和 5-Fu+KSM, 两种方案均能够明显抑制肿瘤发展、提高患者生活质量。但是,化疗药物难免会对患者的机体造成不同程度的损害,不仅影响患者治疗的依从性,而且易导致病情恶化[6-8]。因此,选择一种更为科学、合理、有效的化疗方案治疗恶性滋养细胞肿瘤具有重要的意义。为了提高恶性滋养细胞肿瘤的临床疗效,我们通过本研究分析不同治疗方案的安全

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性及有效性,为相关临床研究提供参考。

1 资料与方法

1.1 一般资料

选取 2010 年 8 月 -2012 年 12 月我院收治的恶性滋养细胞肿瘤患者 58 例,年龄 20-42 岁,平均年龄为(30.4± 1.8)岁。患者入院当天均经绒毛膜促性腺激素测定及组织病理学活检确诊。纳入标准:患者无心、肝、肾等重要脏器损伤;无原发性或继发性精神障碍;无化疗禁忌症;知悉并自愿签署同意书。利用随机数字表法将入选的 58 例患者分为研究组和对照组,每组各 29 例。两组年龄、病情及肿瘤分期等一般资料无明显差异(P>0.05),具有可比性。

表 1 两组患者的基本资料

Table 1 The general data of patients in the two groups

Group	Case	Age(year)	Invasive hydatidiform mole	Horiocarcinoma		
				Ⅱ	Ⅲ	Ⅳ
Study	29	29.3± 1.6	12	5	8	4
Control	29	31.5± 1.9	11	7	7	4
X^2/t		t=1.234	X^2=1.847	＞0.05		
P	＞0.05	＞0.05	＞0.05			

Note: compared between two groups, P>0.05

1.2 治疗方法

1.2.1 **对照组采用 5-Fu+KSM 方案治疗** 静脉滴注氟尿嘧啶 26~28 mg·kg^{-1}·d^{-1}、更生霉素 6 μg·kg^{-1}·d^{-1},持续 8 天。以 8 日为一个疗程,每次治疗需间隔 3 周。

1.2.2 **研究组采用 EMA-CO 方案治疗**[9] 第 1 天:静脉滴注依托泊苷 100 mg/m^2、放线菌素 -D0.5 mg 及甲氨蝶呤 100 mg/m^2,持续 12 小时;第 2 天:静脉滴注依托泊苷 100 mg/m^2、放线菌素 -D0.5 mg 及四亚叶酸钙 15 mg;第 3 天:肌内注射四亚叶酸钙 15 mg,每次 /12 h;第 4-7 日休息;第 8 天:静脉注射长春新碱 1.0 mg/m^2、环磷酰胺 600 mg/m^2;第 9-14 日休息;14 日为一个疗程。

1.3 评价指标

1.3.1 **疗效评价**[10] 根据治疗第 8 周末时患者临床症状的改善情况及辅助检查的结果对临床疗效进行评价,具体标准为:①完全缓解:临床症状全部消失;经 CT、盆腹腔超声检查确定肿瘤转移灶全部消失;每周进行 1 次血清β-hCG 检查,连续 3 次检查结果显示为正常。②部分缓解:患者临床症状有所改善;影像学检查发现肿瘤病灶减小程度达 50%以上;3 次血清β-hCG 值呈对数水平下降,但仍高于正常值。③病情稳定:患者临床症状无好转;影像学检查显示病灶缩小程度小于 50%;血清β-hCG 值下降或上升低于正常值的 10%。④病情进展:患者临床症状出现加重;影像学结果显示病灶增大为原来的 25%或出现了新病灶;血清β-hCG 值呈显著上升趋势。治疗总有效率 = (完全缓解 + 部分缓解)/ 例数。

1.3.2 **毒副反应** 参照 WHO 毒性反应分级标准,评价两组患者在治疗第 4 周时白细胞数量、恶心呕吐等胃肠道反应及口腔溃疡等免疫系统的变化情况。

1.4 统计学方法

采用 SPSS19.0 软件进行统计分析,计量资料以均数± 标准差表示,数据采用 t 检验,计数资料采用卡方检验,等级比较根据符号秩和检验,以 P<0.05 为差异具有统计学意义。

2 结果

2.1 两组患者的临床疗效

如表 2 所示,研究组完全缓解 16 例,部分缓解 7 例,病情稳定 4 例,病情进展 2 例,治疗总有效率为 79.3%;对照组完全缓解 14 例,部分缓解 8 例,病情稳定 5 例,病情进展 2 例,治疗总有效率为 75.9%。两组患者的临床疗效无显著差异(P>0.05)。

表 2 两组患者临床疗效比较

Table 2 Comparison of the clinical effects of patients between two groups

Group	Case	Complete remission	Partial remission	Stable	Progressive	Total effective rate
Study	29	16	7	4	2	79.3%
Control	29	14	8	5	2	75.9%

Note: Z=1.364, P>0.05.

2.2 两组患者毒副反应程度

如表 3 所示,研究组患者白细胞减少:Ⅰ级 12 例,Ⅱ级 10 例,Ⅲ级 7 例;呕吐:Ⅰ级 20 例,Ⅱ级 8 例,Ⅲ级 1 例;口腔溃疡:0 级 23 例,Ⅰ级 2 例,Ⅱ级 3 例,Ⅲ级 1 例。对照组患者白细胞减少:Ⅰ级 2 例,Ⅱ级 11 例,Ⅲ级 16 例;呕吐:Ⅰ级 7 例,Ⅱ级 12 例,Ⅲ级 10 例;口腔溃疡:0 级 2 例,Ⅰ级 3 例,Ⅱ级 9 例,Ⅲ级 15 例。研究组患者治疗后的毒副反应的程度比对照组轻,差异显著且具有统计学意义(P<0.05)。

表 3 两组患者毒副反应程度比较

Table 3 Comparison of the degree about the adverse reactions of patients between two groups

Group	Case	Leukopenia reduction			Vomiting			Oral anabrosis			
		Ⅰ	Ⅱ	Ⅲ	Ⅰ	Ⅱ	Ⅲ	0	Ⅰ	Ⅱ	Ⅲ
Study	29	12	10	7	20	8	1	23	2	3	1
Control	29	2	11	16	7	12	10	2	3	9	15
X2	-	6.397			7.364			8.013			
P	-	<0.05			<0.05			<0.05			

Note: compared between two groups, P<0.05.

3 讨论

从病理学角度考虑，恶性滋养细胞肿瘤是高度恶性的肿瘤，是导致女性不孕不育的因素之一。近年来，国内外专家学者对恶性滋养细胞肿瘤的临床治疗方案展开研究，并获得了一些成果[11,12]。其中，5-Fu 联合 KSM 方案成为临床应用最为普遍的治疗手段，该方案对患者病情的缓解率可达 80~90%[13]。虽然 5-Fu+KSM 能够有效缩小病灶的面积，但化疗药物产生的骨髓抑制、消化道反应等毒副作用十分明显，若不及时进行对症处理可能并发伪膜性肠炎等更为严重的并发症，对患者的身心造成严重影响，而且 5-Fu 联合 KSM 方案的疗程较长，患者不宜耐受[14,15]。此外，癌症患者通常对自身病情的敏感度较高，一旦出现严重的不良反应，往往会采取消极的态度进行治疗，甚至中断化疗，严重影响预后转归[16]。因此，探寻一种安全性较高、病人依从度好的化疗方案目前已经引起医务人员的重视。

据相关文献报道，EMA/CO 方案在治疗恶性滋养细胞肿瘤方面效果较佳且安全性较高[17]。本研究结果显示，两组患者临床疗效差异无统计学意义 (P>0.05)，说明 EMA/CO 方案与 5-Fu+KSM 方案对恶性滋养细胞肿瘤的临床疗效具有很高的一致性。另外，化疗所诱发的毒副反应是影响患者能否坚持治疗的关键因素。5-Fu+KSM 化疗方案治疗周期较长，且毒性损伤程度趋向于Ⅲ级，对患者健康状况的伤害极大[18]。本研究中，采用 EMA/CO 方案治疗的研究组患者的毒副反应程度低于对照组(P<0.05)，说明大多患者可耐受，提高了患者治疗的依从性，进而提高了治疗效果。据统计，截至目前为止尚未发生一例因采取 EMA/CO 治疗方案而致死的情况[19]。我们分析认为 EMA/CO 化疗方案为多要联合，共同作用于病灶，其毒性反应可预测且易于处理，患者也可耐受。但 EMA/CO 方案亦会产生恶心、呕吐等胃肠道反应或口腔溃疡等免疫系统受损的毒副作用，因此，对患者实施该化疗方案的同时应积极做好对症治疗，降低毒副反应程度，进而提高化疗的效果[20]。

综上所述，EMA/CO 方案对于恶性滋养细胞肿瘤的治疗具有积极的意义，其安全性高、毒副反应程度低等特点使患者治疗的依从性和积极性进一步提高，有利于获得更好的疗效，值得进一步推广及应用。

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