·临床研究·

影响经动脉子宫颈癌热灌注化疗临床疗效的多因素分析

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摘要 目的:探讨宫颈癌热灌注化疗栓塞的治疗作用及对临床疗效的影响因素分析。方法:对34例宫颈癌病人进行子宫动脉热灌注化疗及栓塞术,分析肿瘤病理类型,肿块大小,周围浸润及淋巴结转移情况等因素对介入治疗的影响。结果:经过对临床疗效的多因素分析肿块大小对治疗效果影响最大,其次为病理类型。其余影响较小。结论:宫颈癌热灌注化疗栓塞术是治疗宫颈癌的一种适合疗法,尤其适用于肿块较小的病人。可以使疾病得到有效控制,增加手术机会。

关键词:宫颈癌 温热灌注化疗 栓塞 经动脉

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Multiple Clinical Factors analysis for Transcatheter Arterial Hyperthermic Perfusion Chemotherapy of Uterine Cervical Cancer

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ABSTRACT Objective: To evaluate the effects of intra-arterial hyperthermic perfusion chemotherapy for uterine cervical cancer, and to analyze which factor influencing the response to the chemotherapy. Methods: Thirty-four patients with cervical cancer were enrolled in this study. Heating intra-arteray chemothyrapy was performed using cisplatin-based regimens. The response was assessed by ultrasound and examination of surgical specimens. Results: Clinical response was achieved in 28 (82%) patients. Twenty-eight of the 38 parametrial halves were free from cancer. No lymph node metastases were found in eight patients. Initial tumor volume was found to be an independent, significant determining factor of the response to the therapy. Pathological type is another fator which influnce the intervention therapy. Conclusion: Intra-atery hyperthermic perfusion chemotherapy for cervical cancer is useful for the tumor reduction. Tumor volume is a significant determining factor for the response to intra-artery hyperthermic perfusion chemotherapy of uterine cervical cancer

Key words: Uterine cervical cancer; Hyperthermic pefusion chemotherapy; Embolision; Transartery

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宫颈癌是育龄妇女的常见妇科肿瘤性疾病。宫颈癌目前治疗多采用介入化疗栓塞及手术的方法,已被证明取得较好疗效[1,2]。即发现宫颈癌病人于Ⅱb前行介入新辅助化疗及栓塞术,介入后7天手术。而对于Ⅱb后的病人行介入治疗后参照复查结果重新进行分期,如果病灶缩小局部侵犯消失可以手术的则进行手术治疗,如仍不能手术的病人则行放疗或化疗。

我院自2003年来开展对宫颈癌的经动脉热灌注新辅助化疗及栓塞术取得了较好的疗效。但对于影响其治疗效果因素还有待于进一步分析,以明确合适的适应症,掌握适当的治疗时机。

1 材料与方法

1.1 一般资料

本院自2003年开始使用经动脉热灌注化疗栓塞的方法治疗宫颈癌病人34例,病人的年龄在24-69之间平均年龄为(45.6岁),病例类型为鳞癌25例,非鳞9例。按FIGO分期为IB-IVB。

1.2 仪器与方法

飞利浦DSA血管机,seldinger法穿刺右侧股动脉,插入5.0F cobra导管,借助泥鳅导丝将导管超选至子宫动脉。DSA动态采集子宫动脉造影图像。可见宫颈肿瘤显影。灌注药物:顺铂60mg,5-FU1000mg,丝裂霉素16mg。单侧半量加热43度稀释后依次灌注。自制明胶海绵颗粒栓塞子宫动脉。

2 结果评价

采用妇科检查配合超声检查来综合评价肿瘤治疗后的反应情况,在经过动脉热灌注化疗栓塞治疗前后,观察包括患者组织学类型、肿瘤大小、周围侵犯、淋巴结肿大等情况的改变,对这些因素进行回顾性分析,来分析影响宫颈癌热灌注介入治疗疗效的主要因素。分析表明,肿瘤直径是决定肿瘤介入热灌注化疗的主要因素。肿瘤病理类型对介入治疗也产生部分影响。其他因素影响不大。

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表 1 介入治疗后以肿瘤平均缩小率对治疗效果评价

Table 1 The treatment effect evaluation After interventional therapy with the average tumor regression rate

Category	Case	The everage of tumor regression	P 值
Type of orgnization			
Squamous cell carcinoma	25	88.2	0.16
Non- squamous cell carcinoma	9	68.0	
The next invasion			
No	7	85.5	0.39
Yes	27	82.2	
Lymph node metastasis			
No	17	82.3	0.48
Yes	17	83.5	
Tumor volum			
$<80CM^3$	27	88.6	0.007
$\geq 80CM^3$	7	60.9	

3 讨论

宫颈癌是妇科常见的恶性肿瘤，发病率占女性生殖器官恶性肿瘤的首位，病死率在所有女性恶性肿瘤中仅次于胃癌居第二位。患者以 40-60 岁者多见。长期以来，手术和放疗作为主要治疗措施在宫颈癌的治疗中占据主导地位。而化疗被用于治疗晚期和复发性宫颈癌，处于辅助性和姑息性治疗的地位。近年来介入治疗宫颈癌已发展成为第三大治疗手段，并因其创伤小、副反应少优于前两者而被广泛看好。现在已经逐渐形成了以介入 + 手术、介入 + 放疗、介入 + 手术 + 放疗等多种综合性治疗方法，但因为宫颈癌病人在接受治疗时在病理类型、病因、发病年龄、分期等方面均存在不同，因此预后也有很大区别。理论上来说，施行子宫动脉热灌注化疗和栓塞治疗的好处在于缩小肿瘤的体积，期别，降低周围组织，淋巴结和远处转移，以利于下一步进行基本的妇科手术和放疗[3-5]。大量的临床研究结果显示，以顺铂为基础的同步放化疗综合治疗，成为中晚期宫颈癌的标准化治疗模式[6-10]。Jones 等[11]的一项临床实验亦用 DDP 周疗联合局部热疗及放疗治疗晚期宫颈癌 12 例，其中 10 例临床缓解和局部病灶的控制，Bergs 等[12]回顾了热疗、顺铂和放疗三者联合治疗的临床前研究及临床应用，认为Ⅰ/Ⅱ期临床试验结果表明，，三者联合治疗各种癌症种类是有效和可行的，毒性可以耐受的。在此基础上，我们认为以顺铂为主的化疗药物配伍进行宫颈癌的经动脉热灌注化疗栓塞对病人的治疗效果会更加理性。并在实际应用中印证了这一理论。国内亦有学者报道热灌注化疗治疗的宫颈癌病人与普通灌注化疗病人在临床治疗效果上具有统计学差别，热灌注效果明显优于普通灌注病人，且对宫颈及宫旁肿块缩小显著[13]。

我们这个研究的目的是为了对那些施行了热灌注治疗的子宫颈癌患者提供一个量化评价，以分析哪些因素影响介入化疗的效果来决定哪些人更适合行热灌注化疗及栓塞治疗。事实证明肿瘤的直径在肿瘤的治疗中起主要作用。直径较小的肿瘤治疗效果要明显优于直径大的肿瘤，另外，肿瘤组织学来源对预后也有一定的影响作用。这与我们当初的预想是吻合的[14-16]。

子宫动脉热灌注化疗及栓塞临床有效率为 85%-100%，显示出通过这种治疗手段可以使肿瘤明显缩小。此项介入治疗后肿瘤的平均缩小率为 94.4%，也就是说肉眼所见的肿瘤基本消失。这与以前报道的病理学完全有效率在 15%-30%之间相符合[17-19]，部分接受外科手术的病人在外科手术后病理证实在病理学上呈完全有效，即未见恶性细胞。

另外经我们临床研究对比发现宫颈癌热灌注化疗的病人较之普通灌注化疗的病人术中反应轻微，灌注药物时疼痛减轻，术后反应较少。腹痛，腹胀现象及恶心，呕吐现象均有不同程度减低。分析原因可能与热灌注化疗肿瘤血管扩张，药物刺激降低有关。但目前尚无明确报道。

我们有三例病人介入后出现盆腔局部血肿，因此动脉灌注前，中应该确保导管放置轻柔，头端到位，避免粗暴和导管头端顶在血管壁上所造成的损伤，这样可以避免一些严重并发症的发生[20]。宫颈癌病人一般子宫动脉宫颈分支血管均有不同程度增粗，但也有许多纤细的阴部血管分支，如导管头端为小分支开口处且栓塞时手推栓塞剂压力过大亦会造成小血管破裂。因此术中推注造影剂时要先以小剂量低压缓慢推注，待明确无细小分支时方可加大剂量。

总之，子宫动脉热灌注化疗栓塞是治疗宫颈癌的方法之一，尤其对于早期病灶直径较小的肿瘤治疗意义显著，可以使肿瘤明显缩小，增加病人手术机会。

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