

黄蜈散治疗宫颈糜烂的临床研究

山西医学院第一附属医院妇产科中西医结合组

内容提要 分组对比观察黄蜈散治疗宫颈糜烂的临床作用及其对宫糜修复过程的影响,发现黄蜈散治疗组显效率(85.5%)显著高于清洁处理组(18.5%)和无处理对照组(10.8%)。黄蜈散具有消炎、消肿、促进宫糜局部正常鳞状上皮再生,加快宫糜自然修复的作用,对宫颈组织无明显腐蚀和破坏,并不引起宫颈间质的异常纤维化。

1975 年 11 月至 1980 年 11 月,我科用黄蜈散治疗 970 例宫颈糜烂(简称宫糜)患者,治愈率为 64.4%,总有效率为 98.9%。远期疗效观察,复发率为 4.6%^①。治疗 71 例宫颈核异质患者,总逆转率为 100%^②。为了进一步探讨黄蜈散治疗宫糜的临床作用及其对宫糜修复过程的影响,从 1981 年 8 月,我们设计了宫糜局部用黄蜈散治疗、清洁处理和不予处理、只随访观察三种方法,分别对 25~55 岁的 163 例宫糜患者进行宫糜局部 25 次处理或为期三个月的观察,对比其疗效。并通过阴道镜和宫颈活体组织病理检查对各处理组患者宫颈局部变化进行连续观察,对比其异同,现报告如下。

材料与方法

一、研究对象。为 600 例防癌普查妇女中之宫糜患者 163 例,年龄 25~55 岁,宫颈细胞学涂片巴氏 I、II 级。遵照群组配对的原则。以年龄和宫糜范围(分度)为分组标准。将其中 89 例重、中度宫糜患者分为三组,即乳酸加

黄蜈散治疗组、单纯黄蜈散治疗组和清洁处理对照组(简称清洁处理组),另将 74 例轻度宫糜患者不予处理,作为无处理对照组。

二、黄蜈散的药物组成^③。黄蜈散方:黄柏 65%,蜈蚣 6.4%,雄黄 13%,轻粉 13%,冰片 2.6%。共研成极细末,密闭存藏。

三、疗效标准。初次检查后三个月,或局部处理 25 次后行阴道镜检查,糜烂面全部被覆鳞状上皮者为显效;糜烂面部分为鳞状上皮覆盖,但仍有部分柱状上皮者为无效;宫糜范围较初诊时扩大,自觉症状加重者为恶化。

结 果

一、黄蜈散治疗组、清洁处理组和无处理对照组间疗效比较

为了解黄蜈散对宫糜的治疗作用,在限定的时间(处理三个月时),对黄蜈散治疗组、清洁处理组和无处理对照组的 163 例患者分别进行阴道镜复查。并用 Ridit 分析法比较三组间疗效,结果见表 1。

表 1 黄蜈散、清洁、无处理对照三种方法处理宫糜患者三个月时疗效对比

	疗 效 比 较 (例)				Ridit 分析			
	显效	无效	恶化	合计	Ridit 值	例数	SR	95%可信区间
黄蜈散治疗组	53	9	0	62	0.2697	62	0.0733	0.1964~0.3430
清洁处理组	5	19	3	27	0.6129	27	0.1111	0.5018~0.7240
无处理对照组	8	57	9	74	0.6517	74	0.0671	0.5846~0.7188
合 计	66	85	12	163				

注:标准组 Ridit 值=0.500, Ridit 值小表示疗效好

Ridit 分析结果表明, 黄蜈散治疗组疗效显著优于其它两组。清洁处理组和无处理对照组疗效较差。后两组间差异无统计学意义。

二、乳酸加黄蜈散治疗组、单纯黄蜈散治疗组和清洁处理组间疗效比较

表2 乳酸加黄蜈散、单纯黄蜈散和清洁处理三种疗法处理宫颈糜烂患者25次时疗效比较

	疗效比较 (例)				Ridit 分析			
	显效	无效	恶化	合计	Ridit 值	例数	SR	95%可信区间
乳酸加黄蜈散治疗组	28	5	0	33	0.3960	33	0.1005	0.2955~0.4965
单纯黄蜈散治疗组	24	5	0	29	0.4064	29	0.1072	0.2992~0.5136
清洁处理组	5	22	0	27	0.7276	27	0.1111	0.6169~0.8387
合 计	57	32	0	89				

注: 标准组 Ridit 值=0.6728, Ridit 值小表示疗效好

Ridit 分析结果表明: 乳酸加黄蜈散和单纯黄蜈散组疗效显著优于清洁处理组。但乳酸加黄蜈散组与单纯黄蜈散组间差别无显著性意义。

三、窥器视诊和阴道镜观察下的宫颈糜烂修复形式

治疗期间, 用阴道镜对 89 例重、中度、乳头型或颗粒型宫颈糜烂患者进行连续观察, 发现乳酸加黄蜈散组、单纯黄蜈散组和清洁处理组患者, 其宫颈糜烂局部鳞状上皮再生和修复形式与 Dexeus 所描述的宫颈糜烂自然修复形式相同^[9], 取以糜烂边缘开始为主的弥漫性鳞状上皮再生、以糜烂边缘开始为主的局部鳞状上皮再生和以宫颈糜烂区鳞状上皮岛为主的鳞状上皮再生三种形式。

虽然, 乳酸加黄蜈散组、单纯黄蜈散组与清洁处理组宫颈糜烂患者的宫颈糜烂修复形式大致相同。但同年龄组, 同宫颈糜烂面积和类型的黄蜈散治疗组与清洁处理组相比, 后者宫颈糜烂患者修复过程较长, 鳞状上皮再生速度较缓慢, 偶可观察到鳞状上皮再生停滞或柱状上皮重新替代再生之鳞状上皮的现象。

值得提出的是, 在整个观察期间, 89 例宫颈糜烂患者宫颈局部未观察到异形上皮, 异型血管影和不典型上皮再生的表现。

四、宫颈活体组织病理检查结果

为了解乳酸和黄蜈散对宫颈糜烂愈合的影响, 在宫颈糜烂局部处理 25 次时复查, 比较乳酸加黄蜈散组 (用 1% 乳酸溶液浸泡棉球擦拭宫颈和阴道后再上药), 单纯黄蜈散组和清洁处理组之疗效, 并经 Ridit 分析法处理, 结果见表 2。

随意选择治疗前年龄、宫颈糜烂面积和类型相同的单纯黄蜈散组和清洁处理组患者各 10 例, 行治疗前和治疗 25 次时活体组织病理检查。光镜下观察结果显示, 治疗前两组患者的宫颈切片, 其被覆上皮均为单层柱状上皮; 间质内均有腺体和不同程度的炎细胞浸润和水肿。治疗 25 次时, 单纯黄蜈散治疗组患者宫颈切片中被覆上皮鳞化发生率 ($10/10$) 显著高于清洁处理组 ($2/10$) ($P=0.004$), 间质腺体消失率 ($9/10$) 也明显高于清洁处理组 ($0/10$) ($P=0.00005$); 间质炎细胞浸润和水肿程度较清洁处理组轻微 ($P<0.05$)。这提示黄蜈散对宫颈糜烂局部组织有消炎、消肿和促进正常鳞状上皮再生的作用。

五、黄蜈散与电熨术治疗宫颈糜烂的异同

迄今医者多用电熨等物理方法治疗宫颈糜烂。为了了解电熨与黄蜈散对宫颈糜烂局部组织作用异同, 我们用观察黄蜈散组同样的方法连续观察 3 例电熨术治疗的宫颈糜烂患者。发现电熨术是通过电熨热凝作用, 使宫颈糜烂局部发生较大面积凝固性坏死。随着坏死组织的脱落, 可见平滑的上皮由外向内伸展。术后约一个月, 整个宫颈粉红色, 原糜烂区被覆菲薄、平滑的上皮。组织学检查可见被覆上皮有从单层柱状、单层立方至单层扁平上皮的连续移行过程, 并可见储备细胞增生和增殖。偶可见个别细胞核大, 异染质颗粒粗大, 边集及核分裂象。这提示电

熨后上皮增生活跃, 并表明电熨后宫颈局部组织的修复可能与鳞化过程有关。电熨术后三个月和六个月, 宫颈阴道部均为粉白色鳞状上皮被覆。组织学检查被覆上皮为鳞状上皮, 间质有多量胶原纤维增生。细胞成份较少, 与电熨术作用相比, 黄蜈散对宫颈糜烂组织细胞无明显腐蚀和破坏作用, 并不引起宫颈间质的异常纤维化。

讨 论

一、黄蜈散治疗宫颈糜烂的修复过程

阴道镜检查结果表明, 黄蜈散治疗组的宫颈糜烂患者, 其宫颈糜烂局部鳞状上皮再生的形式与宫颈糜烂自然修复的形式相同。但清洁处理组和无处理对照者的结果中, 可看到宫颈糜烂边缘反复发生的修复与糜烂的交替, 使宫颈糜烂状态持续存在。宫颈糜烂修复过程的长短受宫颈糜烂面积、类型和宫颈糜烂边缘形态的影响。轻度宫颈糜烂可通过自然修复过程达到完全愈合。而重、中度宫颈糜烂, 由于糜烂面积大、碱性分泌物多及暴露在宫颈阴道部的柱状上皮易受阴道病原体的感染等因素的作用, 故不易通过自然修复达到完全愈合。乳头型、尤其是宫颈糜烂边缘清晰、整齐, 呈壕沟状者, 其鳞状上皮再生缓慢, 需给予临床治疗。

二、黄蜈散对宫颈糜烂愈合过程的作用

临床资料表明, 黄蜈散治疗组的疗效显著优于清洁处理组 ($P < 0.05$), 阴道镜检查证实, 黄蜈散治疗的宫颈糜烂局部, 其鳞状上皮再生的速度较清洁处理组快。治疗 25 次时组织病理学检查所见, 黄蜈散治疗组被覆上皮的鳞化发生率明显高于清洁处理组; 间质炎细胞浸润和水肿程度较清洁处理组轻微。这提示黄蜈散可能具有消炎、消肿和促进正常鳞状上皮再生的作用。清洁处理组之所以疗效较差, 可能是由于宫颈局部组织炎症反应和局部感染妨碍了正常鳞状上皮形成。

我们的实验亦证实了黄蜈散浸剂对金黄色葡萄球菌、乙型链球菌、大肠杆菌、粪产碱杆

菌、变形杆菌、乳酸杆菌、丁酸梭形厌氧芽胞杆菌及白色念珠菌等有抑制作用。鉴于宫颈糜烂与病原体感染有关, 而当宫颈糜烂存在时, 子宫颈碱性分泌物增多, 易引起或加重阴道正常菌群失调及致病性微生物的感染, 从而影响宫颈糜烂区鳞状上皮再生。黄蜈散有抑制、杀灭阴道内常见细菌的作用, 则可减少宫颈糜烂局部的感染, 有利于宫颈糜烂的修复。

三、鳞状上皮化生的预后

形态学观察结果表明, 宫颈糜烂修复的过程即为鳞状上皮化生的过程。Dexcus^③认为鳞化分为生理性化生和与宫颈原位癌有关的非典型性化生。Adolf Stafl^④认为鳞状化生初期的激活性细胞有吞噬细菌、病毒或其它任何颗粒的能力。并强调此期是进展为成熟鳞状上皮或导致细胞转化为宫颈癌的危险的关键时期。如果阴道内有突变原存在, 例如 HSV-2 或任何一种含有 DNA 的因素, 都可使这些激活的化生细胞转化。

我们的临床研究说明宫颈糜烂与 HSV-2 可能有一定关系。药物实验又证明了黄蜈散浸剂对体外 HSV-2 颗粒有直接灭活作用, 还能降低 HSV-2 诱发小鼠阴道疱疹的死亡率。提示黄蜈散对 HSV-2 感染可能有预防和治疗作用。这也可能是该药能治愈宫颈糜烂和宫颈核异质的药物机理之一。鉴于宫颈癌的病因目前尚不清楚, 故黄蜈散能否通过对细菌和 HSV-2 杀灭、抑制作用, 减少或预防非典型化生的发生, 达到治疗核异质和预防宫颈癌发生的目的, 仍有待于进一步研究。

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Abstracts of Original Articles

Experience in TCM-WM Treatment of the Side Effects of Trophoblastic Tumor Chemotherapy

Cui Guifen (崔桂芬)

Beijing Obstetrics and Gynecology Hospital, Beijing

A total of 30 cases and 61 courses treated with TCM-WM were compared with 41 courses without TCM therapy. The patients were divided at random into three groups. Group 1 were treated with TCM during the course of chemotherapy. Group 2 were treated with TCM after the course. Group 3 were treated with WM only. The chemotherapy was carried out with 5Fu 25-26mg/kg and combined with Actinomycin 5-6 μ g/kg for 8 days or 5Fu 25-30mg/kg for 10 days or Actinomycin 7-9 μ g/kg for 10 days respectively. According to the diagnosis and treatment with TCM, the side effects were divided into 3 types, namely, upwardly perverse Qi of the stomach, endogenous heat due to deficiency of Yin, and deficiency of both Qi and Yin. The effectiveness of each type treated with a definite recipe was observed.

The unchanged rates of leukocyte in the 3 groups were 75.6%, 40%, 41.6% and those of the blood platelet were 95.1%, 70%, 78.1% respectively. It showed that the results of group 1 was significantly higher than the others ($P < 0.05$). There were only two cases (4.8%) with serious side effects in the digestive tract, but no serious ulcerative stomatitis and high fever in group 1. The differences were significant between group 1 and the other two groups ($p < 0.01$). (Original article on page 202)

The Late Effect of Gossypol Treatment in Gynecological Diseases — A Clinical Study of 72 Cases

Wang Youfang (王友芳), et al

Department of Obstetrics and Gynecology, Capital Hospital, Chinese Academy of Medical Sciences, Beijing

The late results of 72 cases of gynecological diseases after discontinuation of gossypol treatment are reported. The longest follow-up period was 4 years. There were 31 cases of myoma, 14 of adenomyosis, 14 of endometriosis and 13 of myoma or adenomyosis with endometriosis.

The late effect was satisfactory. The action was sustained and reversible. Amenorrhea continued for half a year in 63.6%, and for one year in 10.0%. After discontinuation of medication, menstruation returned within half a year in 80.4% of the cases. The symptom and sign usually improved: the effective rate of uterine bleeding was 47.1%, dysmenorrhea 58.1%, reduction of myoma size 63.0% and reduction of endometriotic nodules 58.3%.

The recurrence of dysmenorrhea was related with the length of the course of treatment, clinical stage and the estrogen level of vaginal smear recovered. The recurrence of myoma and bleeding was related with age and their pretreatment estrogen level.

There was no side-effect in the follow-up study. The action of gossypol is similar with danazol. Sharp vigilance must be maintained on the possibility of hypokalemia. (Original article on page 205)

A Clinical Study of Huang Wu San (黄蜈散) on the Treatment of Cervical Erosion

*TCM-WM Research Group, Department of Gynecology and Obstetrics,
First Teaching Hospital of Shanxi Medical College, Taiyuan*

In order to study the clinical effect of Huang Wu San (HWS) on the treatment of cervical erosion and its influence on the repair process, the clinical records were treated with statistical analysis. The results showed a very significant difference between the HWS group (62 cases, effective rate 85.5%) and the cleaning control group (27 cases, effective rate 18.5%) as well as between the HWS group and the control group (74 cases, effective rate 10.8%). As there is no difference between the last two groups, it is confirmed that HWS is an effective drug for external treatment of cervical erosion. During treatment, 89 cases with cervical erosion, which had been classified into papillary and follicular erosion types and the extent of which fell into 3 and 2 degrees, were observed with vaginoscope successively. The results revealed that the regeneration and repair processes of squamous epithelium at the cervix after using HWS or cleaning were the same as the natural regeneration and repair processes of cervical erosion. Only the processes of the former were faster than the latter.

It has been proved by histopathological examination that HWS has no necrotic and destructive effect on the cervical tissue and does not cause abnormal fibrosis of the cervical interstitial substance, but abates inflammation and swelling and helps regenerate the normal squamous epithelium. However, there is coagulation necrosis in the area of the operation at the cervix after electric cauterization. There is a considerable amount of collagenous fiber proliferation in the cervical interstitial substance from the third month to the sixth month after operation.

(Original article on page 208)