

金龙蛇口服液合参麦注射液对中晚期胃癌患者 肿瘤标志物和免疫功能的影响

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摘要 应用中药金龙蛇口服液及参麦注射液治疗中晚期胃癌患者 35 例,并应用化疗的 16 例患者对照。结果应用中药治疗的患者,体力指数(Karnofsky 评分)及 NK 细胞活性明显升高,CD₄、CD₄/CD₈ 亦明显升高,CD₈ 明显下降,与治疗前比较差异均有显著性($P<0.05$),而化疗组除 CD₄/CD₈ 略有改善外,NK 细胞活性、CD₃、CD₄ 较治疗前下降。两组肿瘤标志物 CEA 及 CA₁₉₋₉ 也有一定程度下降,但与治疗前比较无明显差异($P>0.05$)。提示中药金龙蛇口服液及参麦注射液联合应用治疗中晚期胃癌有良好作用。

主题词 胃肿瘤/中药疗法 参麦注射液/治疗应用 @ 金龙蛇口服液

中晚期胃癌患者,临床常采用放化疗进行治疗,但由于患者体质因素及各种并发症,难以耐受放化疗。要求采用中医药治疗。我们应用金龙蛇口服液及参麦注射液治疗中晚期胃癌患者,发现其能明显提高患者生存质量,降低肿瘤标志物水平,并对机体免疫功能发挥调节作用。现将观察结果报告如下。

1 临床资料

观察病例均为近年来我科住院及门诊病人,男性 33 例,女性 18 例,平均年龄 63.2 岁,肿瘤发生部位:胃体部 26 例,胃窦部 10 例,贲门部 15 例;病理类型:管状腺癌 30 例,低分化腺癌 11 例,印戒细胞癌 3 例,粘液腺癌 5 例,未分化腺癌 2 例。观察病例中手术后患者 28 例,均为复发或发生转移者。全部病例临床分期为Ⅲ、Ⅳ期患者。以上病例分为两组,中药组 35 例,其中男性 23 例,女性 12 例,平均年龄 62.0 岁,平均体力指数(Karnofsky 评分)为 51.14,均为不能耐受化疗或不愿化疗的患者;化疗组 16 例。其中男性 10 例,女性 6 例,平均年龄 62.9,平均体力指数为 53.75,两组年龄、性别及体力指数等情况基本一致,两组比较无明显差异($P>0.05$)。

2 治疗及观察方法

2.1 治疗方法:中药组:给予金龙蛇口服液(由天南星、半夏、全蝎、蜈蚣、土鳖虫、陈皮、枳实、川贝母、白芥子、鸡内金、甘草等组成,院内制剂,10ml/支),30ml/

次,每日 3 次口服;连用 3 个月;参麦注射液(正大青春宝药业有限公司,10ml/支),40ml/次,每日 1 次静脉滴注;15 天为 1 个疗程,应用 3~5 个疗程。化疗组:采用 FM 方案化疗,MMC 8~10mg 加生理盐水 50ml 静脉注射,第 1 天;5-FU 500~750mg 加 5%葡萄糖 500ml 静脉滴注,第 1~5 天,每 28 天重复 1 周期,应用 3 个周期。以上两组病例有并发症者可给予对症治疗。

2.2 观察方法:生存质量(Karnofsky 评分)评测:肿瘤标志物 CEA、CA₁₉₋₉ 采用 ELISA 法;NK 细胞活性、T 淋巴细胞亚群采用流式细胞仪技术检测。分别在治疗前和治疗后各检测 1 次。

2.3 统计方法:正态分布资料用 t 检验,非正态分布资料用秩和检验。

3 结果

3.1 生存质量评分比较:治疗后中药组 Karnofsky 评分明显升高,与治疗前比较差异有显著性($P<0.001$);而化疗组与治疗前比较明显下降($P<0.05$)。见表 1。

表 1 两组治疗前后生存质量评分比较(分, $\bar{x} \pm s$)

组别	例数	治疗前	治疗后
中药组	35	51.14±11.05	65.71±15.58*
化疗组	16	53.75±9.57	45.63±7.27

* 与治疗前比较, $P<0.001$

表 2 两组肿瘤标志物 CEA 及 CA₁₉₋₉
治疗前后变化比较($\mu\text{g/L}$, $\bar{x} \pm s$)

组别		CEA	CA ₁₉₋₉
中药组	治疗前	145.68±122.49(13)	175.86±137.30(18)
	治疗后	85.61±67.45(13)	121.89±92.44(18)
化疗组	治疗前	141.56±124.93(7)	164.49±130.76(9)
	治疗后	103.21±75.88(7)	117.08±87.15(9)

表中数据后括号内为例数

3.2 两组肿瘤标志物 CEA 及 CA₁₉₋₉ 治疗前后比较:治疗前中药组 CEA(本院正常值为 $<15\mu\text{g/L}$) 高于正常者 13 例,CA₁₉₋₉(本院正常值为 $<37\mu\text{g/L}$) 高于正常者 18 例;化疗组分别为 7 例和 9 例。治疗后两组肿瘤标志物 CEA 及 CA₁₉₋₉ 与治疗前比较均有一定程度降低,但差异无显著性($P>0.05$)。见表 2。

3.3 两组 NK 细胞活性及 T 淋巴细胞亚群变化比

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表3 两组NK细胞活性及T淋巴细胞亚群变化比较($\bar{x} \pm s$)

项目	中药组(35例)		化疗组(16例)	
	治疗前	治疗后	治疗前	治疗后
NK(%)	13.93±7.20	18.08±8.38*	13.04±6.65	11.88±6.81
CD ₃ (%)	60.39±9.35	66.39±8.05*	61.45±8.90	57.89±8.89
CD ₄ (%)	36.44±8.14	41.66±6.97*	35.63±7.84	34.77±7.73
CD ₈ (%)	32.44±6.45	27.87±7.59*	31.84±7.84	30.03±6.45
CD ₄ /CD ₈	1.19±0.42	1.61±0.53*△	1.22±0.56	1.23±0.45

*与本组治疗前比较, $P < 0.05$; △与同项目化疗组比较, $P < 0.05$

较:治疗前中药组与化疗组各项指标比较无明显差异($P > 0.05$)。应用金龙蛇及参麦注射液治疗后(中药组)NK细胞活性明显升高,CD₄及CD₄/CD₈亦明显升高,CD₈明显下降,与治疗前比较差异有显著性($P < 0.05$)。化疗组NK细胞活性、CD₃、CD₄、CD₈与治疗前比较略有下降,CD₄/CD₈有所上升,但无明显差异($P > 0.05$)。治疗后中药组CD₄/CD₈与化疗组比较差异有显著性($P < 0.05$)。见表3。

4 讨论

由于中晚期肿瘤已发生局部或远处转移,多数患者已无手术治疗的可能,并且由于患者体质虚弱,或有各种并发症,患者难以耐受化疗和放疗,因此恶性肿瘤晚期常缺乏有效的治疗方法,对此类患者应以提高患者生存质量、减轻患者痛苦、延长生存时间为治疗目的。因此患者生存质量是评价中晚期肿瘤治疗有效与否的标准。研究表明,免疫系统的所有效应成分均对消除肿瘤细胞、控制肿瘤生长有作用。其中NK细胞被认为是宿主抵抗原发或转移部位肿瘤细胞生长的第一道防线。T淋巴细胞亚群是宿主抗肿瘤免疫反应中起主导作用的免疫细胞之一。肿瘤的发生、发展与以T细胞为中心的细胞免疫功能失调有密切关系。在肿瘤的形成和发展中产生或分泌的免疫抑制因子可诱导CD₈亚群的形成与成熟,同时阻止CD₃、CD₄细胞亚群的形成与成熟,CD₈细胞所产生的可溶性因子可抑制免疫活性细胞的细胞毒效应,有利于肿瘤的生长和转移。而CD₄能促进效应细胞发挥抗肿瘤作用。在肿瘤患者中T淋巴细胞亚群比例失调,提示患者免疫功能失调,抗肿瘤效应减弱。从我们观察的结果来看,应用中药金龙蛇口服液及参麦注射液治疗的中晚期胃癌患者,其生存质量较治疗前明显升高;NK细胞活性、CD₄、CD₄/CD₈比值均明显上升($P < 0.05$),而采用化疗的患者生存质量、NK细胞活性、CD₃、CD₄较治前下降。从而说明金龙蛇口服液和参麦注射液合用对于提高患者的生存质量,增强患者免疫功能有显著的作用。

研究表明,CEA及CA₁₉₋₉与肿瘤的浸润深度、淋巴结转移及远处转移明显相关^[1,2],观察CEA及

CA₁₉₋₉的变化对判断预后具有重要意义。我们用金龙蛇口服液及参麦注射液治疗后,患者CEA及CA₁₉₋₉较治疗前有一定程度下降,提示金龙蛇口服液与参麦注射液合用可能对抑制肿瘤发展和转移有较好的作用。

胃癌在中医学领域归属于“胃脘痛”、“胃反”、“积聚”等范畴。中医学认为,其形成和发展受内、外两种因素影响。脏腑功能失调、气血虚弱、正气不足为其内因,痰浊瘀毒积聚、气滞血瘀是其外因。在其发病过程中正邪两方面不断变化,早期以邪实为主,晚期则以正气不足、气血亏虚占主要地位,因此扶正祛邪是治疗肿瘤的基本大法。

金龙蛇口服液是我科魏品康教授经过长期临床实践总结出的治疗消化道肿瘤的有效方药。我科曾单独应用金龙蛇口服液治疗消化道肿瘤,并与单纯化疗及金龙蛇口服液合化疗者对照,发现其可以提高NK细胞活性及T细胞亚群水平,减轻化疗的副作用^[3]。金龙蛇口服液由天南星、半夏、土鳖虫、蜈蚣、全蝎等药物组成。天南星、半夏燥湿化痰、消肿散结;土鳖虫破积抗癌、逐瘀通络;全蝎、蜈蚣可解毒散结。全方是针对痰浊瘀阻是肿瘤发生的重要原因而制定的。具有消痰破瘀、解毒散结通络的作用。药理学研究表明,天南星、半夏、土鳖虫、全蝎、蜈蚣等对胃癌、肝癌等癌细胞均有杀伤和抑制作用。参麦注射液由人参、麦冬组成。人参功效大补元气;麦冬可养阴润肺、益胃生津;两药合用具有扶助正气、增强机体祛邪能力的作用。药理研究认为,本药可以激活调节机体免疫功能,提高T细胞总数,降低白细胞介素-2受体含量,提高NK细胞活力,并可降低肿瘤细胞内LDH活性,提高瘤细胞内cAMP/cGMP比值,抑制肿瘤细胞生长。

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ABSTRACTS FROM ORIGINAL ARTICLES

Clinical Observation on Treatment of 288 Cases of Correlative Gastric Diseases Infected by Pyloric Helicobacterium with Kang Wei Granules

Chen Feisong, Wei Beihai, Yao Wei, et al.

Kang Wei Granules which can strengthen the spleen, replenish Qi, clear away heat and remove dampness was used to treat 288 cases of correlative gastric disease infected by pyloric helicobacterium. Seventy-four cases were treated with triple therapy (Bismuth being the mainly ingredient) as control group. Results indicated that the treatment group was significantly superior to the control group in improvement of main symptoms, especially for the types of deficiency of spleen and stomach, and internal accumulation of dampness-heat ($P < 0.05$). There was no significant difference between the two groups in gastroscopy, pathological examination and the positive grade of pyloric helicobacterium ($P > 0.05$). It is suggested that Kang Wei Granules has a better clinical therapeutic effect for treatment of correlative gastric disease infected by pyloric helicobacterium.

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Key words: Gastric diseases/microbiology infection of pyloric helicobacterium/ Chinese drug therapy @Kang Wei Granules
(Original article on page 599)

Effects of Jin Long She Oral Liquid Combined with Shen Mai Injectio on Tumor Marker and Immunological Function in the Patient of Intermediate and Late Gastric Cancer

Qin Zhifeng, Wei Pinkang, Li Xiangyong

Jin Long She Oral Liquid combined with Shen Mai Injectio was used to treat 35 cases of intermediate and late gastric cancer as treatment group, and chemotherapy was used to treat 16 cases as control. Results indicated that the index of physical strength (Karnofsky score assessment) and natural killer (NK) cell activity in the treatment group increased significantly, CD₄, CD₄/CD₈ increased and CD₈ decreased as compared with those before treatment ($P < 0.05$). In the chemotherapy group besides CD₄/CD₈ improved slightly, NK cell activity and CD₄, CD₈ decreased; tumor marker CEA and CA₁₉₋₉ decreased to a certain degree in the two groups, with no significant difference compared with those before treatment. It is suggested that combination of Jin Long She Oral Liquid and Shen Mai Injectio has a good effect on intermediate and late gastric cancer.

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Key words: Gastric tumor/traditional drug therapy Shen Mai Injectio/therapeutic use @Jin Long She Oral Liquid
(Original article on page 605)

Effect of Administration of Herba Epimedii at the Optimal Time on Levels of Sexual Hormones

Wang Fei, Zheng Yang, Xiao Hongbin, et al

In order to confirm the theory of administration at the optimal time in *The Yellow Emperor's Internal Classic*, effects of administration of Herba Epimedii at the optimal time on the level of sexual hormones in young mice were investigated to explore the relationship between the time of administration and the effect. Results indicated that (1) Yin Yang Huo Decoction had sexual hormone-like actions, increasing weight of uterus and serum estradiol (E₂) content in the female mice, increasing serum testosterone (T) content in the male mice; (2) The administration at Mao (the period of the day from 5 a. m. to 7 a. m.) and You (from 5 p. m. to 7 p. m.), hours influenced the increases of uterus weight and serum E₂ content in the female mice and serum T content in the male mice to a certain degree, the action at Mao being stronger than that at the You. It is suggested that administration for tonifying the kidney and strengthening Yang in the early morning has the best effect.

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Key words: Sexual hormones/metabolism Herba Epimedii
(Original article on page 619)

Cytologic Study on Prevention and Treatment of Primary Osteoporosis with Chinese Drugs for Tonifying the Kidney

Shi Yinyu, Zhan Hongsheng, Zhao Yongfang, et al.

In order to compare differences of effects of complex prescription for reinforcing the kidney on osteoblast (OB) and osteoclast (OC), MTT method was used to determine proliferous capability of OB, bone lacuna count was used for quantitative assessment of absorbent activity of OC. Results showed that the mean influencing rate of Jin Gui Shen Qi Pill, Bu Shen Yi Jing Prescription, Zhi Bai Di Huang Pill, and Western medicine Premarin tablet for proliferous capability of OB was 159.2%, 121.5%, 21.6% and 75.7% respectively; the mean influencing rate for bone lacuna count was 50.2%, 21.0%, 19.8% and 38.1% respectively, suggesting that the drug for even reinforcing Yin and Yang can improve proliferation of OB and inhibit activity of OC, and increase of the drug for warming Yang can strengthen the promoting action on proliferation of OB, but increase of the drug for nourishing Yin had opposed action, the drugs for nourishing Yin plus the drugs for purging the pathologic fire can inhibit activity of OC and proliferation of OB.

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Key words: Osteoporosis/bone and bone tissue/cytology
(Original article on page 621)