丹参对恶性淋巴瘤患者高血浆纤维蛋白原的影响

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内容提要 对35例恶性淋巴瘤患者分组治疗，结果表明丹参对COP治疗方案有增效作用。血浆纤维蛋白原（Fg）测定显示恶性淋巴瘤患者组较正常对照组高（$P<0.01$）。COP方案治疗组疗后血浆Fg较疗前有所降低（$P>0.5$）；丹参—COP方案治疗组血浆Fg疗后较疗前明显降低（$P<0.01$）。血浆Fg含量与疗效呈负相关。提示丹参的促纤溶作用是其抗肿瘤作用的重要机制之一。

我们用丹参加化疗治疗恶性淋巴瘤患者22例，并对患者进行了治疗前后血浆纤维蛋白原的检测，疗效较单用化疗的13例满意，报告如下。

临床资料

35例恶性淋巴瘤患者，男性30例，女性5例。年龄最小者3岁，最大者60岁，其中3～15岁8例，16～30岁8例，31～40岁4例，41～50岁9例，51～60岁6例。35例均经病理证实，病理类型：何杰金氏病6例，非何杰金氏淋巴瘤29例。

方法

一、分组方法：对入院的患者按Richard Doli方法进行随机分组。一组接受COP方案治疗，另一组用丹参—COP方案治疗。按Rye会议的分期标准，COP方案治疗组的13例中ⅠA 1例，ⅡA 4例，ⅣA 5例，ⅣB 3例。丹参—COP方案治疗组的22例中ⅠA 1例，ⅠB 2例，ⅡA 5例，ⅡB 4例，ⅣA 2例，ⅣB 8例。用Wilcoxon方案进行统计学处理后，$P>0.05$，两组患者病情没有明显差别，具有可比性。

二、治疗方法：COP方案：环磷酰胺400mg静脉注射，每周2次；长春新碱1mg静脉注射，每周1次；强地松5mg口服，每日3次。连续用药3周，休息1周后继续用药3周为观察疗程。丹参—COP方案：在按COP方案用药期间每日静脉滴注丹参注射液10ml（本院药剂科制备）。

三、检测方法：采用12.5%亚硫酸钠沉淀法测定血浆纤维蛋白原。标本为15例健康者和恶性淋巴瘤患者治疗前后的血浆。

结果

一、临床疗效：疗效评定标准按1978年全国抗癌药物会议（常州）的标准略加修改[1]。COP方案组：完全缓解（CR）1例，部分缓解（PR）8例，稳定（S）3例，进展（P）1例。丹参—COP方案组：CR 4例，PR 18例。用Wilcoxon方法进行统计学处理，两组间疗效的差异具有显著性意义（$P<0.05$），即丹参—COP方案疗效优于COP方案。

二、血浆纤维蛋白原（Fg）检测结果：健康对照组血浆Fg含量（g/L）为2.1385±0.1682，恶性淋巴瘤患者组为3.3196±3.6038，二者差别非常显著（$P<0.01$），即恶性淋巴瘤患者有高血浆纤维蛋白原的特点。COP方案组治疗前为2.803±1.596，治疗后为2.591±0.646，疗后血浆Fg有所降低，差异无统计学意义（$P>0.5$）。丹参—COP方案组治疗前为3.625±1.638，治疗后为2.343±0.576，疗后血浆Fg较疗前明显下降（$P<0.01$）。两组患者疗后血浆Fg均降低，可以看出患者血浆Fg含量与临床疗效呈负相关。COP治疗可以使患者血浆Fg含量减少，丹参—COP治疗，减少更为明显。

讨论

丹参（*Salvia miltiorrhiza* Bge）的抗癌作用可能是多方面的[2]，其中一个方面可能与其调整患者血凝—纤溶—血小板系统的紊乱有关。恶性肿瘤患者，血液呈高凝状态，凝血物质中纤维蛋白原，Ⅰ、Ⅴ、Ⅶ、Ⅷ、Ⅸ、Ⅺ因子增加，血小板数及血小板活性均增加；抗凝物质中抗凝血酶Ⅲ、C蛋白（Protein C）减少；纤溶机能低下，纤溶酶原的绝对量减少而且活性

减低；抗纤溶活性增加，α_1抗胰蛋白酶（α_1-antitrypsin）、α_2巨球蛋白（α_2-macroglobulin）增加，抗纤溶酶活性增强。高凝状态是由于肿瘤宿主凝血—纤溶—血小板系统紊乱的结果[3~5]。一些肿瘤细胞自身可以产生凝血活酶样物质，在血小板凝集物质介入下能够诱导血栓形成，从而促进肿瘤细胞在末梢血管壁着床。在此情况下，肿瘤周围形成了纤维蛋白网，对肿瘤有保护作用，并可对付宿主机体免疫监视系统。在血栓形成过程中血小板凝集放出各种增殖因子（PDGF、TGF、EGF）[6]，这些因子可能有促进肿瘤在着床部位增殖的作用。高转移株瘤细胞对上述增殖因子反应性高是由于该细胞株有较多的增殖因子受体。

恶性肿瘤患者的血栓症包括肿瘤血栓和非肿瘤血栓。在肿瘤着床、增殖中有重要意义的是肿瘤血栓。纤维蛋白原是形成肿瘤血栓的主要因素。Baserga 应用电子显微镜及免疫荧光技术发现纤维蛋白在早期转移肿瘤床形成中的作用。我国著名血液病学家陈悦书曾指出：恶性淋巴瘤患者的血浆纤维蛋白原常有增加。我们也观察到这种现象。John 等曾指出抗凝剂可以增强机体对抗肿瘤细胞转移、增殖的能力，并有利于抗癌化疗药物和辐射治疗更好地发挥作用。肝素、华法令、纤溶酶原活化剂用于抗癌治疗的研究受到了重视，并取得一些研究成果[7]。

丹参—COP方案治疗组的患者应用丹参后提高了化疗药物的抗肿瘤活性。这种增效作用与患者高血浆纤维蛋白原向正常化下降是有联系的，这种联系可能与丹参的促纤溶作用有关[8]。

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冠心病血瘀证发病机理初探

——与A型行为类型及血浆TXB_2、6-Keto-$PGF_{1\alpha}$的关系

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为探讨前列腺素系统及A型行为类型在冠心病血瘀证发生中的作用，我们对84例确诊为冠心病患者，按中医辨证分型，分为血瘀证组64例、非血瘀证组20例。另设正常对照组11例。用放射免疫法测定其血瘀TXB_2、6-Keto-$PGF_{1\alpha}$水平，并以张伯源制定的A型性格问卷，判定其行为类型。

结果：血瘀证组血浆TXB_2为270.31±287.5(pg/ml M±SD，下同)，比非血瘀证组（129.25±53.80）和对照组（109.24±49.06）明显增高，P均<0.05。血浆证组血浆6-Keto-$PGF_{1\alpha}$为234.86±101.72，明显高于对照组（160.71±51.17），P<0.05，与非血瘀证组(189.87±72.61)比较，无明显差异。血瘀证组与非血瘀证组TXB_2与6-Keto-$PGF_{1\alpha}$变化均呈良好的正相关，r分别为0.566(n=33)、0.651(n=21)，P均<0.01。且两组的TXB_2/6-Keto-$PGF_{1\alpha}$比值，分别为1.13±0.68、0.73±0.31，P均<0.05。

行为类型：47例血瘀证患者，A型性格者18例(38.38%)，非血瘀证组2例(10.00%)，P<0.05。在20例A型行为类型患者中，血瘀证者18例(90.00%)，非血瘀证者2例(10.00%)。本实验比较了A、B、M行为类型的血瘀证患者血浆TXB_2和6-Keto-$PGF_{1\alpha}$变化，发现A型性格者TXB_2水平有增高趋势。

上述结果提示：TXB_2、6-Keto-$PGF_{1\alpha}$代谢平衡失调，在冠心病血瘀证的发病中起重要作用，是血瘀证病理生理改变的生化基础。A型行为类型，可能是血瘀证发生的诱发因素。

Clinical and Experimental Study of Xuefu Zhuyu Tang(血府逐瘀汤) in Treating Qi(气) Stagnation and Blood Stasis Type of Hyperlipidemia

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Xuefu Zhuyu Tang (XFZYT,血府逐瘀汤) was used in 20 cases of hyperlipidemia with Qi stagnation and blood stasis syndrome (QSBS). The results were that the symptoms of QSBS have markedly improved, and the levels of serum TC and TG have decreased, especially on TG ($P<0.001$). It showed that QSBS was probably in certain connection with increasing serum lipids, and XFZYT could decrease them. The results of experiment were as follows: the regulating Qi (RQ) herbs, a component in XFZYT, decreased the levels of serum TC, TG, LDL-ch, and liver tissue's TC in hyperlipidemic rats; the promoting blood circulation (PBC) herbs, another component in XFZYT, decreased the levels of liver tissue's TC, TG and liver index on hyperlipidemic rats; XFZYT had the effect of both components, it decreased either the levels of serum TC, TG and LDL-ch, or the liver tissue's TC, TG and liver index. So we consider that RQ and PBC herbs in XFZYT probably work in coordination on regulating the metabolism of lipids.

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Clinical Observation of Three Lianas Syrup in Treating 302 Cases with Various Types of Lupus Erythematosus

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302 cases with various types of lupus erythematosus(LE), including 58 cases of chronic discoid LE (DLE), 23 cases of subacute cutaneous LE (ScLE), 180 cases of systemic LE (SLE), 10 cases of overlapping LE (OLE) and 31 cases of mixed connective tissue diseases (MCTD) were treated with Three Lianas Syrup (TLS). Improvement after treatment was observed in 288 cases (95.4%) within 1~3 weeks, arthralgia, fever and skin lesions were greatly improved. The visceral involvment and immunological parameters was also improved. Decrease of dosage or withdrawal of corticosteroid was also an aspect of improvment. The therapeutical effect of TLS was better than any other control group. Above data showed that TLS inhibited the polyclonal antibody strains of B cells and improved the regulation of antibody formation. TLS may activate cellular immunity especially NK cells, which are important in immune surveilance in LE and the activation of NK cells perhaps is the essence of pharmacological action of TLS.

(Original article on page 604)

Effect of *Salvia miltiorrhiza* on Hyperfibrinogen in Patients with Malignant Lymphoma

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35 cases of malignant lymphoma were divided into two groups randomly, 22 cases of which were treated with *Salvia miltiorrhiza* (SM)–COP therapy, and only 13 cases by COP therapy. In terms of short-term effect, it has been found that SM–COP therapy was more effective than COP therapy, $P<0.01$. The experimental study showed that one of the mechanisms of SM against tumor is improving the hypercoagulation state through lowering the serum hyperfibrinogen, from 3.626 ± 1.638 to 2.343 ± 0.576 mg/dl, $P<0.01$, which is significant in showing that promoting the fibrinolytic activity was closely related with the therapeutic effect, and was one of the antitumor mechanisms.

(Original article on page 607)

Observation on CT Changes in Patients with Cerebrovascular Disease Treated by Kangcu(抗卒) Pill

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126 patients (1987–1988) with cerebrovascular disease were treated with kangcu pill (KCP) which is mainly consisted of leech, in comparison with a non-KCP control group of 45 patients. KCP was given orally in daily dosage of 1.5~3 g. Both groups were provided with comprehensive basic therapy. A 30~35 days therapeutic course were carried out. The effective rate of KCP in relieving symptoms is 97.6%, while the control group 88.9%. CT were performed in some patients before and after one therapeutic course. The effective rate of KCP in CT changes is 88.4% (61/69), while 65.2% (15/23) in the control group. The difference was significant in CT responses ($X^2=4.94$, $P<0.05$). KCP is superior to the control group. The KCP was beneficial to perifocal tissue and caused the focus changing in density or even disappearing on CT. It could prevent the semidark perifocal area and becoming the dark area, reduce the damage and necrosis of the brain tissue. Hence, recovered the neurological functions, three types of CT dynamic changes of ischemic cerebrovascular disease were being put forward.

(Original article on page 609)