甜菊治疗高血压病的临床观察

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内容提要　本文应用国产甜菊甙治疗高血压病31例，并以23例高血压病患者服安慰剂作对照。每次甜菊甙0.5g，一日三次口服，30天为一疗程。结果显效18例（58.1%），有效8例(25.8%)，无效5例(16.1%)，总有效率83.9%；对照组有效率为8.6%。两组差异非常显著(P<0.01)。服药后未发现血脂升高，副作用亦少而轻。其降压机制尚待研究，可能与利尿有关。

1984年，我们应用新疆甜菊叶治疗高血压病，取得了初步疗效[1]。但甜菊叶浸剂内服，尚有许多缺点。为进一步验证疗效及改进剂型，最近我们应用成都市制药化学厂生产的甜菊甙治疗高血压病，其疗效优于甜菊叶，且副作用少，现将结果报告于下。

材料和方法

一、病例选择：在心血管病防治点石河子八一糖厂，对已确诊高血压病(按WHO诊断标准，不包括临界高血压)的61例，随机分为治疗组(31例)和对照组(30例)；在治疗观察过程中，对照组有7例采用其他降压治疗故删去，本组仅统计23例。

治疗组31例，男17例，女14例；年龄38～74岁，平均50.5岁；高血压病Ⅰ期13例、Ⅱ期16例、Ⅲ期2例；病程1～25年，平均10.9年。

对照组23例，男10例，女13例；年龄46～73岁，平均51.2岁；高血压病Ⅰ期16例，Ⅱ期6例，Ⅲ期1例；病程1～20年，平均8.2年。

二、治疗药物：治疗组采用成都市制药化学厂生产的S-70型甜菊甙，含总甙量80±5%，每次0.5g，一日三次装入胶囊内服，1疗程30天。对照组应用与甜菊甙形状类似的药用淀粉，作为安慰剂，每次0.5g，一日三次亦装入胶囊内服。

三、观察方法与疗效评定：按全国高血压病普查方案要求，测量卧、坐、立位血压，治疗前一周及治疗中，停用其他药物，服药前及服药期间，由专人每周测血压、详细询问病史及查体，并作详细记录；疗程结束后，按全国规定标准，进行疗效评定[2]。显效：(1)舒张压下降10mmHg及以上，并达正常范围；（2）舒张压下降20mmHg及以上，但未达正常。有效：（1）舒张压下降不及10mmHg，但已达正常；（2）舒张压下降10～19mmHg，但未达正常，（3）收缩压下降30mmHg以上。无效：未达到以上标准。

治疗结果

一、降压疗效：见表1，治疗组显效18例(58.1%)，有效8例(25.8%)，无效5例(16.1%)，总有效率为83.9%。其中Ⅰ期高血压病13例，显效9例(69.2%)，有效2例(15.4%)；Ⅱ期高血压病16例，显效8例(50.0%)，有效6例(37.5%)；Ⅲ期2例，显效1例。Ⅰ期高血压病显效率高于Ⅱ、Ⅲ期。

表1　两组降压疗效比较

	显效				有效				无效			
	总例数	Ⅰ期	Ⅱ期	Ⅲ期	总例数	Ⅰ期	Ⅱ期	Ⅲ期	总例数	Ⅰ期	Ⅱ期	Ⅲ期
治疗组 n=31	18	9	8	1	8	2	6	—	5	2	2	1
对照组 n=23	1	—	1	—	1	1	—	—	21	15	15	1

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对照组仅1例(4.3%)显效，1例(4.3%)有效，总有效率为8.6%，与治疗组比有非常显著的差异($P<0.01$)。

二、症状疗效：两组治疗前多数有头痛、头晕、心悸等症状，服药后治疗组症状多消失，而对照组无改变，见表2。

表2 两组症状疗效比较

			头痛	头晕	心悸	头部沉重	颈项紧迫	下肢浮肿
治疗组 n=31	前	例 (%)	14 (45.2)	20 (64.5)	15 (48.4)	1 (3.2)	1 (3.2)	2 (6.4)
	后	例 (%)	—	2 (6.4)	3 (9.7)	—	—	—
对照组 n=23	前	例 (%)	11 (47.8)	18 (78.3)	8 (34.8)	—	4 (17.4)	—
	后	例 (%)	11 (47.8)	18 (78.3)	8 (34.8)	—	4 (17.4)	—

三、心电图疗效：治疗前后均行休息时常规12导联心电图检查。治疗组9例有异常改变，表现为陈旧性心肌梗塞，左心前导联T波倒置，ST段水平样或斜下型压低，左心室肥厚和早搏(室早、联律性及结早)。治疗结束后复查，除1例结早消失外，余同治疗前，未见好转或恶化。对照组4例有异常改变，表现为陈旧性心肌梗塞，ST段斜下型压低，左心前导联T波倒置、双相或平坦、室早(联律性)，服安慰剂前后无变化。

四、血脂变化：见表3。服药30天后，治疗组胆固醇及β-脂蛋白均值似有轻度下降，但无统计学意义。对照组改变不大。说明甜菊甙对血脂无明显影响，未发现有升血脂作用。

表3 治疗前后血脂情况 (M±SD)

		胆固醇(mg%)	β-脂蛋白(mg%)
治疗组	疗前	219.4±52.7*	550.8±114.6*
	疗后	206.1±61.3	533.5±137.0
对照组	疗前	201.8±43.7*	519.9±142.7*
	疗后	209.9±41.8	545.8±165.8

* 同组治疗前后比 $P>0.05$

五、尿量变化：治疗组日尿量均值服药前为1550ml (600～2200ml)，服药后为1790ml (1200～2500ml)，治疗前后差异显著($P<0.01$)。一般于服药24～48小时尿量开始增多，一周后增多较明显。其中10例(32.3%)较服药前平均增加540ml/日(300～900ml/日)，4例夜尿3～4次，总量700～900ml，全日尿量2000～2500ml；另10例尿量稍增多，11例(35.5%)服药前后尿量改变不明显。对照组治疗前日尿量均值为1460ml(1200～2700ml)，治疗后为1500ml (1200～2600ml)，变化不大($P>0.05$)。

六、副作用：服甜菊甙一周后，有4例(12.9%)出现腹胀，2例(6.5%)反酸，1例(3.2%)恶心，2例(6.5%)头痛，均较轻，未经特殊处理，坚持治疗，持续5～7天自行消失。

讨　论

甜菊又名甜叶菊(Steria rebaudiana Bertoni)，菊科，多年生草本，内含有甜菊糖甙，其甜味纯正适口，甜度为蔗糖的300倍。Pomart等试验表明：甜菊甙在人体内不进行代谢，原型排出体外。1970年巴拉圭的医学家在第七届国际糖尿病学会上发表了关于甜菊甙的药效和安全性的报告，认为它对人体无毒害作用，且对高血压、糖尿病有一定疗效[3]。Akashi等对其进行急性、亚急性毒理试验，最高投给量达到每日5 g/kg，对动物无不良影响[4]。国外将其作为天然糖精使用。1977年，我国引种成功，目前许多省区(包括新疆)都已种植。

本组31例高血压病患者，应用国产甜菊甙治疗，总有效率为83.9%，一般服药一周后，血压有较明显下降，显效率达58.1%，对早期高血压病疗效较为显著，未发现有明显的不良反应。因此，我们认为：甜菊甙是值得进一步研究和推广的降压药。

甜菊的降压机制尚待研究，服甜菊甙后，多数患者尿量有不同程度增多，与甜菊叶浸剂观察结果相同[1]，说明它有一定的利尿作用，通过利尿，排钠排水、降低血容量，减少心排血量，这可能是它降压的机理之一。甜菊甙不引起血脂升高，又无严重副作用，这是它优于其他利尿性降压药之所在。

(王伟医师协助本文统计学处理，谨谢)

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川芎消化道给药对犬心肌缺血的影响（摘要）

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川芎(*Ligusticum Wallichii* Franch)为伞形科多年生草本植物的根茎，性味辛温，功能止痛，活血行气，有"血中气药"之称。川芎化学成分与药理作用研究已有不少报道。但消化道给药的实验报道较少。为更符合临床用药习惯，我们进行了消化道给药抗心肌缺血的研究，现将结果报告如下。

材料与方法

动物：健康成年犬，雌雄兼用，体重10～20kg。

药物：(1)生理盐水，北京制药厂制。(2)川芎制剂，本院药厂制，每克制剂相当于生药2.8g。(3)硫氮草酮，日本田边制药株式会社制，批号35090。

方法：动物经戊巴比妥钠(30mg/kg)静脉麻醉，切开气管，插管连接SC型电动呼吸机。左侧第四肋间开胸，做心包床固定心脏，分离冠状动脉左前降支中段以备结扎。放置"多点固定式"心外膜电极，连接RM-6000八导生理记录仪，记录30个点的心外膜电图。

实验共分四组，均经胃管给药。药物剂量见附表。各组于结扎冠脉后15分钟记录心外膜电图作为给药前对照，然后给药，持续结扎冠脉，于给药后的30、60、120、180分钟分别记录心外膜电图，进行自身对照及组间对比。

结　果　结果见附表。生理盐水组2 ml／kg 灌胃后，心肌缺血程度无明显变化，给药后为药前水平的94.2～102.1%。川芎组给药后60分钟，心肌缺血程度明显减轻，为给药前水平的84.7% ($P<0.05$)，给药后120及180分钟，分别为给药前水平的70.0%及49.2%，自身对照及与生理盐水组组间对照均有显著性差异。硫氮草酮小剂量组，心肌缺血程度未见明显改善，大剂量组给药后60分钟开始明显减轻，给药后180分钟作用达高峰，为给药前水平的43.6%，与生理盐水组比较有显著性差异($P<0.05$)。

附表　川芎等胃内给药后犬心肌缺血值的改变

给药剂量		动物数	Σ—ST值(mv) 给药前	给药后 30分	60分	120分	180分
生理盐水	2ml/kg	4	0	2.13	-5.61	-1.44	-0.39
硫氮草酮	2mg/kg	2	0	-3.86	-8.38	5.82	35.09
硫氮草酮	5mg/kg	2	0	-18.76	-44.54 *△	-46.39 *△△	-56.44 * *△△
川　芎	5g/kg	2	0	-1.30	-16.30	-29.98	-50.70

与生理盐水组对比：$*P<0.05$，$**P<0.01$

自身对照：$\triangle P<0.05$，$\triangle\triangle<0.01$

讨　论　以往，国内外在研究抗心肌缺血药时，多采用静脉注射给药，这种给药途径对于成份复杂，常规口服的中药研究不够合理。为了更符合临床用药实际，本实验采用口服给药，虽然这在实验方法学上困难较大，难于观察到阳性结果，为加快吸收速度、提高吸收程度，我们用空腹犬进行实验。经过摸索，建立了较为合理的给药途径及实验方法，并取得较为满意的结果。实验表明，给生理盐水组3小时内，心肌缺血程度无明显变化，说明动物模型可靠，观测指标在较长时间内可保持相对稳定。川芎组由于药物在胃内吸收缓慢，短时间内难于达到有效血药浓度，因而在给药30分钟时尚无明显减轻。药后120～180分钟作用达高峰，并有进一步减轻的趋势，说明消化道给药虽然起效缓慢，但治疗作用明显、持久，可明显减轻心肌缺血，与临床观察结果相符。硫氮草酮大剂量组给药后60分钟开始显效，药后180分钟作用达高峰，作用与川芎组相似，两组无显著性差异。

marked increase in TXB_2 level in comparison with the normal control and the patients with BD syndrome ($P<0.001$). The patients with both BD and BE syndrome showed a marked increase in TXB_2 level comparing with normal group and BD syndrome ($P<0.001$). At the same time the patients with both BD and BE syndrome showed a marked decrease in 6-keto-$PGF_{1\alpha}$ level which is compared with normal persons and BE syndrome ($P<0.01$). The group of BD syndrome, BE syndrome and both BD and BE syndrome showed a significant difference in TXB_2/6-keto-$PGF_{1\alpha}$ ratio in comparing with the normal control; and the TXB_2/6-keto-$PGF_{1\alpha}$ ratio showed a significant difference among the three groups. This result suggested that decrease in the level of 6-keto-$PGF_{1\alpha}$ in plasma might be a characteristic of the BD syndrome. The increase in level of TXB_2 in plasma might be a characteristic of the BE syndrome. However the increase in level of TXB_2 and the decrease in level of 6-keto-$PGF_{1\alpha}$ at the same time also showed that it might be a characteristic of both BD and BE syndrome. The levels of TXB_2, 6-keto-PGF_1 and ratio of TXB_2/6-keto-$PGF_{1\alpha}$ in plasma might be one of the objective parameters for the syndrome differentiation of BD and BE in patients with IHD. The imbalance between TXB_2 and 6-keto-$PGF_{1\alpha}$ in plasma may be one of the basic pathological change in BD and BE syndrome in patients with IHD. To a certain extent, the change of balance regulating system of TXB_2 and 6-keto-$PGF_{1\alpha}$ levels may reflect the interdependence and mutual condition of the physiological function and pathological change of vital energy and blood. Therefore the TXA_2 and PGI_2 in plasma may be the material base of the vital energy and blood.

(Original article on page 15)

Clinical Observation on Treating Hypertensive Patients with Chrysanthemum Morifolium

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Among all the 54 patients suffering from hypertension, 31 were treated with Chrysanthemum morifolium glucoside and the remaining 23 as the control group, a placebo. The dosage was 0.5 g in capsule, three times a day. The course of treatment was 30 days. Hypertension was diagnosed according to the standard of WHO. Measurement of blood pressure and evaluation of therapeutic efficacy were determined by complying with unified national standards and levels. Results: 18 cases (58.1%) were marked effective, 8 cases (25.8%) effective, 5 cases (16.1%) non-effective. The total effectiveness was 83.9% and the control group 8.6%. The difference between these two groups was significant ($P<0.01$). The effectiveness of the first stage hypertensives was more distinct than that of second and third stage. Before and after receiving treatment, the ECG of the patients showed no evident improvement or deterioration. As to blood lipids, the mean value of cholesterol and β-lipoprotein showed a slight reduction and no increase at all. Side-effects such as slight flatulence, acid regurgitation, nausea and headache appeared among a few patients. It was, however, unnecessary to stop medication or taking any other measures. They would disappear by themselves. The amount of urine was increased and the blood pressure decreased evidently one week after taking drugs. Possibly its hypotensive effect was relevant to the diuresis.

(Original article on page 18)

Nitrogen Balance in Uremic Patients Treated with Rhubarb Retention Enema

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It is known that uremic toxic substance can be excreted by GI tract. Recent reports suggested that blood urea nitrogen (BUN) of uremic patients was lowered by diarrhea with rhubarb. In order to evaluate the effectiveness and mechanism of rhubarb on uremia, the nitrogen balance (NB) in five uremic patients treated with rhubarb were studied. All these patients were in stable condition. Their Ccr was 8.70 ± 5.40 ml/min, Scr 10.90 ± 6.90 mg/dl, BUN 75.20 ± 41.50 mg/dl. The treatment was divided into two stages: (1) Control (14.20 ± 3.70 days): Average protein intake was 34.80 g/day. NB was studied for 5.2 ± 1.3 days. (2) Treatment with rhubarb (12.4 ± 3.1 days): Average protein intake was similar to that of control. Retention enema with 10 g/day of rhubarb powder added to 500~700 ml/day of water was used. NB was studied for 5.0 ± 1.2 days. Results: (1) After treatment with rhubarb, BUN was lowered from $62.80+35.50$ mg/dl to 45.00 ± 38.20 mg/dl ($P<0.05$). No changes of Ccr and Scr were found. (2) Average feces nitrogen (FN) during treatment with rhubarb was increased from 1.56 g/day (control) to 2.35 g/day ($P<0.02$). Urine nitrogen (UN) was decreased by 0.30 g/day (from 3.58 ± 0.49 g/day to 3.32 ± 0.67 g/day, $P<0.05$). (3) NB during rhubarb treatment was lower than control ($+0.14\pm0.85$ g/day vs $+0.52\pm1.06$ g/day, $P<0.05$). These results suggested that rhubarb retention enema on reduction of BUN was effective and this effectiveness might be related to decrease of FN by the drug. Because of NB change, the rhubarb treatment might exert harmful effect on the protein metabolism of uremic patients.

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Effect of Herbal Mixture Jiang Qi Ding Chuan San (降气定喘散) on PEFR, HR and BP in Asthmatics

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The folk herbal mixture Jiang Qi Ding Chuan San (JQDCS, 降气定喘散) which has been widely used for the treatment of chronic asthma in Guangzhou. It consists of Ephedra sinice, Semen Sinapis albae, dried