

滋阴补肾药对鸡佝偻病钙磷代谢的影响

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内容提要 实验性佝偻病雏鸡在每日滴喂六味地黄汤浓煎剂条件下,两个月内,血清钙、磷浓度均高于不给药的佝偻病鸡组;而碱性磷酸酶活性则低于不给药的佝偻病鸡组。两个月后,X线诊断证明不给药的佝偻病组严重,患病率高达65.5%,而给药组仅为16.7%。不给药组的胫骨灰分中钙、磷含量明显低于给药组($P<0.05$)。滋阴补肾药物的上述效应机理可能在于药物本身含有麦角骨化醇等天然的抗佝偻病成分,或者由于增强肾的生理功能,调节了钙磷代谢的平衡。

近代医学对中医学“肾主骨生髓”理论的论证,在国内已有阐述^[1,2]。其依据之一是肾脏通过对维生素D的活化以及对钙磷代谢的作用影响成骨作用。虽然中医文献中肾的概念与解剖学上的肾不尽相同,但确实包含了后者的功能。因此,在辨证施治的基础上,用滋阴补肾药物治疗骨质病虽屡有记载,但其机理如何,尚待探讨。本研究主要观察雏鸡在致佝偻病条件下,给予滋阴补肾药物后,对体内钙磷代谢的改变和对佝偻病防治作用。

材料与方法

一、鸡佝偻病模型的制造:参照关庆润等^[3]及刘长山等^[4]的方法塑造模型。实验用雏鸡系石家庄市电解厂的来克种。于孵出后第二天选雄性100只,按饲鸡常规方法饲喂5日,随机分为三组:(1)对照组,(2)佝偻病组,(3)佝偻病给药组(简称给药组)。从第6日起,每组均饲喂缺维生素D饲料。饲料按关庆润等报道的第一种配方^[3],随意食用。对照组每日分上、下午两次在室外放养四小时,接受阳光照射。其余时间在不避光的室内饲养。佝偻病组及给药组均在避光的室内饲养。给药组每日滴喂中药浓缩液两次,每次2~3滴,同时给佝偻病组滴喂蒸馏水2滴。中药配方:熟地、山萸肉、山药、丹皮、云苓、泽泻。按4:2:2:1.5:1.5:15称重,水煎两次,去渣,浓缩。使每毫升含原药2.5g。实验从5月初开始至7月上旬结束。

二、生化测定:自鸡心取血移入微量试管中,放置4℃冰箱中,凝固,离心15分钟(3000转/min)分离血清。血清钙、磷及碱性磷酸酶按上海医学化验所方法^[5]作微量测定。实验结束时,将鸡全部断头,剥

离取胫骨,剔净,在110℃烤箱中烘干5小时,称干重量。在高温熔炉中(600℃)灰化至白色为止(约6小时)称灰粉重量。将灰粉溶解于0.1N HCl 25ml中。按测血清钙、磷方法测定其钙磷含量。

三、X线照像:条件为钼靶,100mA,0.2 S,32~34KV。X线管至胶片距离为76cm。

实验结果

一、血液化学成分的测定:三组鸡于日龄第20、38、52及第67日时各取血一次测定血清钙、磷及碱性磷酸酶活性,从表1可以看出,对照组血清钙为8.1~11.6mg/dl,磷3.4~5.5mg/dl。在日龄20天时,钙磷含量均较低,日后逐渐上升。至52天时血钙达最高峰,为11.6mg/dl。血磷至第67天时达最高峰,为5.5mg/dl。钙磷乘积亦相应地在第52天时出现高峰,为47.7。正常雏鸡血清钙磷含量尚未见文献报道。在哺乳动物,此值应属正常范围。佝偻病组血清钙磷含量与对照组相比明显下降,相差极为显著($P<0.001$)。钙磷乘积在整个实验期间均低于30。给药组血清钙、磷含量虽比对照组稍低,但高于佝偻病组,基本在正常范围。日龄38天时,与佝偻病组相比,相差极为显著($P<0.001$)。钙磷乘积除第20天及第67天测定偏低外,另两次均属正常范围(35.3~36.3)。

血清碱性磷酸酶活性变化结果见表2。其中对照组碱性磷酸酶活性以第一次(鸡龄20天)之值最高,以后逐步下降,至第67天时比第20天时下降约50%。佝偻病组在实验期始终处于较高水平。在第67天时与对照组比,差别极为显著($P<0.001$)。给药组血清碱性磷酸酶活性虽随鸡龄增长而下降,但下降幅度低于对照组,至第67天时比第20天时下降约34%。与佝偻

表 1 三组鸡血清钙、磷含量及钙磷乘积比较

	钙(mg/dl)				磷 (mg/dl)				钙 磷 乘 积			
	20	38	52	67(天)	20	38	52	67(天)	20	38	52	67(天)
对 照 组	8.8±1.0 (19)	10.8±1.1 (15)	11.6±1.6 (15)	8.1±0.9 (15)	3.4±0.8 (17)	3.7±0.9 (18)	4.1±1.5 (29)	5.5±1.6 (15)	30.2 (17)	39.5 (15)	47.7 (15)	44.0 (15)
佝偻病组	7.4±1.3 (33)	7.8±0.7 (26)	7.2±1.3 (21)	7.7±0.9 (25)	4.0±1.3 (33)	2.8±0.5 (26)	3.1±1.5 (18)	3.4±0.7 (18)	29.5 (33)	21.8 (26)	28.7 (18)	26.4 (18)
给 药 组	7.9±1.3 (26)	9.6±0.9 (21)	9.3±1.2 (23)	8.2±0.9 (19)	3.6±0.9 (25)	3.8±0.7 (22)	3.8±1.4 (23)	3.5±1.1 (20)	28.7 (25)	36.3 (21)	35.3 (23)	28.5 (19)

注：括弧中数字为实测鸡数；**为佝偻病组与对照组的t检验， $P<0.001$ ；▲▲为佝偻病组与给药组的t检验， $P<0.001$ ；表内统计数据为 $M\pm SD$ ，下同

表 2 三组鸡血清碱性磷酸酶活性比较

	血清碱性磷酸酶(金氏单位/dl)		
	20天	38天	67天
对 照 组	553.1±258.0 (18)	513.6±277 (14)	265.7±112.5 (12)
佝偻病组	777.9±355.5 (34)	528.3±328.7 (24)	578.5±297.5 (23)
给 药 组	491.8±271.8 (25)	468.7±255 (17)	322.1±182.1 (18)

注：括弧中数字为实测鸡数；**为佝偻病组与对照组的t检验， $P<0.001$ ；▲▲为佝偻病组与给药组的t检验， $P<0.001$

病组相比，在第20、67天时均有显著性差别($P<0.001$)。

二、骨盐测定结果见表3。

表 3 三组鸡胫骨骨盐含量比较

	灰分率%	钙	磷
对照组 (24)	30.0±3.1	104.6±11.6	45.3±6.2
佝偻病组(29)	27.6±3.4*	91.5±8.2**	40.0±5.9**
给药组 (21)	28.3±3.2	96.6±9.0▲	44.0±6.4▲

注：括弧中的数字为实测鸡数(每鸡测一胫骨)。*为佝偻病组与对照组的t检验， $P<0.05$ ；**为佝偻病组与对照组的t检验， $P<0.01$ ；▲为佝偻病组与给药组的t检验， $P<0.05$

对照组鸡骨灰分率($\frac{\text{灰分重}}{\text{骨干重}} \times 100$)为30%，此值可

代表鸡日龄67天时骨中无机盐的百分数。佝偻病组与给药组骨盐的百分率均下降，分别为27.6%及28.3%。但佝偻病组与对照组相比，其差别非常显著。测量灰分中钙磷含量符合上述变化。以上结果均说明在无阳光照射下，骨骼中磷酸钙盐减少。但在给药组，骨中贮积钙磷能力虽低于对照组但却高于佝偻病组。

三、X线照像：后肢骨X线检查，结果见表4。

当鸡龄1个月时，对照组骨质正常者占全组鸡数的100%，给药组仅为20.8%，出现佝偻病征者为79.2%，佝偻主要为早期佝偻病(占62.5%)，未发现重度佝偻病；在佝偻病组，佝偻病阳性率高达90.6%，未见有重度表现，但中度佝偻病的阳性率比给药组高20.8%。当鸡龄60天时，对照组有34.6%发生佝偻病X线征，未有重度表现。给药组的佝偻病阳性率为95.8%，其中重度者为16.7%。佝偻病组则为100%患佝偻病，重度者为65.5%，比给药组高48.8%。

表 4 鸡佝偻病模型X线征阳性率

组 别	鸡日龄	骨质正常 只 %	佝偻病X线阳性征			阳性率%
			早期	中度	重度	
			只 %	只 %	只 %	
对 照	30	16 100	0	0	0	0
	60	17 65.4	6 23.1	3 11.5		34.6
给 药	30	5 20.8	15 62.5	4 16.7		79.2
	60	1 4.2	5 20.8	14 58.3	4 16.7	95.8
佝偻病	30	3 9.4	17 53.1	12 37.5		90.6
	60	0	0	10 34.5	19 65.5	100

注：早期：钙化带模糊、密度低，甚至不能测量。中期：早期钙化带消失，干骺端增宽。重度：干骺端增宽，毛刷状或杯口状

讨 论

隋代巢元方在《诸病源候论》^[1]中的小儿杂病诸候篇中曾对佝偻病的三种主要证候，即解颅候、齿不生候、数岁不能行候有所论述。并归之于肾气不足，在治疗方面以补肾益髓，益气充血为主。本实验取用的六味地黄汤为滋阴补肾方剂。实验结果证明，给药组经每日给药一个月后，血清钙、磷含量均较实验开始时升高，钙磷乘积亦达35~36。虽较对照组仍然偏

低,但远高于佝偻病组。血清碱性磷酸酶活性亦趋向较低水平,这与重度佝偻病阳性率低密切相关。佝偻病组其碱性磷酸酶活性比给药组高1.5~1.8倍,其重度佝偻病阳性率亦高约4倍。给药组中骨钙磷含量按每克骨干重量计算,均较佝偻病组高,其差别有显著性($P<0.05$)。总之,在给药组中,各项生化指标以及X线检查的结果虽不如对照组表现的那样正常,但优于佝偻病组,这可能是药物作用的效果。

体内缺乏维生素D时,滋阴补肾药物能改善钙磷代谢和降低重度佝偻病的阳性率,按近代医学观点尚难以解释。可能与药物中含有抗佝偻病成分(如麦角钙化醇)有关;或者与药物增强肾功能,改善体内保留钙、磷的能力,有利于代偿维生素D缺乏而引起的钙磷代谢的缺陷有关。这些推论有待深入探讨。

(本文鸡胚骨X线照片经河北医学院第三医院放射科王沛教授分析并提供诊断结果,特表谢意)

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脑导水管梗阻致脑积水 1 例治验

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患者李海洋,男,13岁,因阵发性头痛伴呕吐半年,加重半个月,于1983年5月3日入院。患儿右侧颞部有外伤史,右侧头部及头顶持续性隐隐胀痛和间歇抽搐7年,曾诊断外伤性癫痫。

入院检查: T: 37.8°C, P: 80次/分, R: 24次/分, BP: 102/60mmHg; 颈部可扪及一蚕豆大淋巴结; 心肺(-), 腹部平软, 肝脾未扪及, 胸透正常; 血沉: 28mm/h; WBC: 16000; N: 71%, L: 29%; 脑脊液: 压力 $>400\text{mmH}_2\text{O}$, 无色, 微浑, 潘氏试验+++; RBC 50个/ mm^3 , WBC 150个/ mm^3 , 糖40~50mg%, 氯化物640mg%; 疑诊为结核性脑膜炎, 经抗痨加激素治疗两周, 头痛、呕吐止, 体温正常出院。以后继续抗痨三个月, 病情加重, 头颅膨胀, 疑脑积水于同年9月初经湖南医学院附属一院神经外科颅脑超声波检查, 考虑颞叶后位占位性病变; 脑室造影, 导水管梗阻(以炎症粘连可能性大)。同年10月初回本院诊治。患儿垂头闭目, 形寒肢冷, 低吟头痛不已, 口唇紫绀, 神志朦胧呈危重病容, 舌质淡, 苔薄白, 脉沉细无力, 脑积水类似中医学“解颅”。

治疗方法: 西医对症支持疗法: 10%葡萄糖500ml内加地塞米松10mg、10%氯化钾10ml、速尿20mg静脉滴注, 间隔2天输1次, 共9次。有发热、感染时, 肌注青霉素80万u, 1天2次, 连用5~7天。中医辨证: 脾肾阳虚, 治宜温补脾肾, 化瘀逐水; 拟方真武汤加味: 生芪30g, 党参、白术、茯苓、当归、川芎、泽泻各10g, 炒附片、甘草先煎各5g, 三七5g(用开水磨, 调兑均匀), 1日3次服, 每天1剂, 共服18剂。患儿精神、饮食逐渐好转。再诊: 舌质齿龈有瘀斑点, 舌苔稍黄, 脉细沉; 更方: 通窍活血汤加减: 赤芍、川芎、桃仁、红花、穿山甲、地龙、生芪各10g, 红枣五枚, 生姜三片, 老葱白五根煎服, 三七磨调(方法同上), 共10剂; 头痛减轻, 呕吐止。三诊, 前方去地龙、姜、葱、枣, 加柴胡、牛膝、生地、当归、枳壳各10g为基本方, 再加三棱、莪术, 或五灵脂、蒲黄各10g, 或水蛭、蜈蚣各3g, 共服50剂。头痛等症消失, 坚守原方随证加减又进30剂巩固治疗。共治疗4个月后, 经湖南医学院附属一院复查, 近期痊愈; 又随访2年多未复发。

Ultrastructural Observation on Experimental Fracture Treated with Principle of Promoting Blood Circulation and Relieving Stasis — A Transmission Electron Microscopic Study

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In the course of healing the standardized fracture of radius in 50 New Zealand rabbits, an expeditious effect on repairing was achieved as a result of administration of *Radix Salviae miltiorrhizae* which exerted the action of promoting the blood circulation and relieving the stasis. X-ray study of the radial fracture revealed that callus formation appeared earlier and was denser as compared with another series of 50 control rabbits. As judged from the transmission electron microscope (TEM) observation, the favourable effects could be reflected in five aspects. Firstly, there was an increase in both the site of distribution and the number of the osteogenic cells. Secondly, the fibroblasts, in addition to their change in configuration, showed very active protein synthesis. There was also an expedition of the normal process of fibroblast degeneration. Thirdly, there was appearance of increased number of osteoclasts in different localities of fracture callus to promote remodelling. Fourthly, there was exuberant amount of collagen fibril formation in enhancing the production of the organic matrix. Fifthly, there was numerous dense calcium granules in the swollen mitochondria of the fibroblasts so as to provide adequate supply of calcium for the calcification of the matrix vesicles and the collagen fibrils.

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Antiviral Efficacy of the Extract of *Luffa cylindrica* Vine in Vivo and in Vitro

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The antiviral activity of the extract of *Luffa cylindrica* vine (ELCV) on virus infection in vivo and in vitro was studied. Results from the study indicated that: (1) The mice resulted in a 66.7 ~ 80 % protection when the ELCV was given to mice prior to infection with Japanese encephalitis virus, but only a weak protection of the treated mice could be observed when given after infection; (2) The ELCV was highly active in inducing resistance to cytopathic changes in primary rabbit kidney cell cultures challenged with vesicular stomatitis virus; (3) Interferon was induced in rabbit by intravenous injection with the ELCV. The circulating serum interferon level peaked at 2 hr after injection; (4) The antiviral activity of the ELCV was greatly lowered by heating at 100 °C for 45 min. and was partially resistant to RNase at concentration of 20 µg/ml; (5) Ultraviolet spectrum of the ELCV revealed a pattern of nucleic acids.

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Effects of Kidney Yin (阴) Tonic on Calcium and Phosphorus Metabolism in Rickety Chickens

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100 chickens of 7 days after birth were divided into three groups randomly: The control group (I), the rickets group (II), the rickety chicken treated with kidney Yin tonic "Liuwei Dihuang decoction 六味地黄汤" (III) twice daily. All of them were fed with vitamin D-free diet. The group II and III were bred in darkroom except group I. Serum calcium and phosphorus concentration and alkaline phosphatase activity were determined once every two weeks. A significant reduction of mean calcium and phosphorus concentration and an increased alkaline phosphatase activity were observed in group II in comparison with group I and group III in certain periods. After two months, X-ray diagnosis also showed that the incidence of severe rickets in group II (65.5 %) was higher than that in group III (16.7 %). The mean calcium contents (mg/g of dry bone weight) in tibia of the three groups were 105, 92 and 97 respectively (I/II $P < 0.01$, II/III $P < 0.05$) and the phosphorus contents were 45, 40 and 44 respectively (I/II $P < 0.01$, II/III $P < 0.05$). The findings indicated that the tonic lowered the incidence of severe rickets might contain some natural anti-rickets components such as ergocalciferol or enhance the function of the kidney in regulating calcium and phosphorus balance.

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