实验研究

糖皮质激素建立老年大鼠骨质疏松症模型的实验研究

上海宝钢冶金建设公司职工医院（200941）
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摘要　通过对老年期前雄性 SD 大鼠肌注地塞米松注射液，利用糖皮质激素的促骨质吸收作用，观察了实验鼠的全身骨密度、骨小梁容积及生物力学抗弯强度三项指标在高、中、低三种剂量中的变化。结果表明，中剂量地塞米松连续肌注 6 周后，骨的抗弯强度、骨密度及骨小梁容积都显著降低（$P<0.05$），低剂量虽已有降低趋势，尚无统计学意义（$P>0.05$）。认为用介乎中、高剂量之间的量 0.25mg/100g 体重每周 2 次，连续 6 周可建立老年性大鼠骨质疏松症模型。

关键词　糖皮质激素　骨质疏松症　病理模型

自 Kalu[1] 1989 年建立标准化绝经后骨质疏松症大鼠病理模型之后，近年来有关骨质疏松之药理实验病模几乎都以此方法建立[2]。此方法为雌鼠切除卵巢，其症状类似人类女性绝经后骨质疏松症。但以现行这种方式造模研究药理及病理机制对于临床老年男性骨质疏松症似不太理想。为建立另一种骨质疏松模型，我们依据糖皮制激素对骨质的促吸收作用[3~6]，进行了不同剂量的糖皮质激素对诱发雄性大鼠骨质疏松效果的实验研究，报导如下。

材料与方法

1. 材料

（1）动物：雄性 SD 大鼠，11 月龄，体重 400±20g，32 只（上海中医药大学实验动物中心提供，合格证号：沪医实动单项准第 65，66 号，1995 年合格）。

（2）药物：地塞米松酸钠注射液（上海第九制药厂生产，批号：931208，规格：5mg/ml）。

（3）仪器：Lunar 双能 X 线骨密度测定仪（USA），附动物全身骨密度测定软件一套；INSTRON－1122 万能材料试验机（England）；VIDAS 全自动图像分析仪（England）。

2. 方法：32 只大鼠随机分为 4 组，第Ⅰ组为正常对照组，正常喂养，给予与造模组等容积的盐水肌注，2 次/周；第Ⅱ、Ⅲ、Ⅳ组分别为低、中、高剂量地塞米松注射组，剂量依次为 0.05、0.1、0.4mg/100g 体重，肌肉注射，2 次/周。

上述方法处理 6 周后处死动物。处死前测量骨密度。处死后，取右侧胫骨做病理切片，进行骨小梁容积观测；取股骨做生物力学抗弯强度试验。

结果

1. 外观变化　对照组毛发光洁，活动体态正常。低剂量组稍次；中高剂量组有不同程度的精神萎靡，活动迟缓，躲避反应迟钝，毛发稀疏。

2. 死亡情况　高剂量组死亡 2 只，其它组无死亡。

3. 骨密度、生物力学抗弯强度及骨小梁容测定结果见表 1。

上述三种测定项目的结果与地塞米松剂量高低的相关分析为：r_1：－0.854；r_2：－0.51；r_3：－0.88。r_1、r_2、r_3 分别为骨密度，抗弯强度及骨小梁容积与地塞米松剂量的相关系数。

讨　论

本组观测的三项指标中，骨密度是量化骨矿含量最客观的指标之一，骨密度明显降低可作为骨质疏松模型形成和评价防治效果的指标之一[7]；骨小梁容积是骨的形态计量学指标，可直观描述骨丢失状况，当有统计学意义的骨小梁减少时，即可认为骨质已疏松；生物力学抗弯强度的降低在相应的临床表现为老年人易为轻微外力发生骨折。本实验结果表明：注射低剂量激素时，各指标均呈降低趋势，但无统计学意义差异；中剂量激素则出现有统计学意义的减少；高剂量则各数据的降低均有显著的统计学意义。从相关分析上看，除抗弯强度不显著，骨密度与骨小梁容积与激素剂量均呈显著负相关（r 分别为－0.854 和－0.88），表明骨质

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的丢失与激素剂量成正比。病理切片光镜下可发现，松质骨的小梁被吸收严重而皮质骨却保存尚好。可否认为激素促进骨质吸收以松质骨为主而非皮质骨，表现为生物力学降低程度不如骨密度和骨小梁容积。

上述实验结果证实，用 0.1mg/100g 体重地塞米松肌注老年期前雄性大鼠，2 次/周连续 6 周可形成大鼠骨质疏松模型。考虑大鼠的种及体质等各种因素，结合 Olgaard[6] 和彭国瑞[8] 的报导，为保证模型的高成功率及低死亡率，我们认为最佳造模剂量应为 0.25mg/100g 体重。此剂量约为 Olgaard[6] 报导 90 天成模剂量的 4 倍多，又远低于彭国瑞的最小长期应用激素的致死量，为本实验成模剂量的 2.5 倍又小于本实验的高剂量。11 月龄的大鼠，生理上接近人类老年期前，模型造成后，与非绝经后骨质疏松症有较多的生理、病理可比性。况且因素比较单一，容易控制其他偶然因素，死亡率较低，模型成功率较高。

表 1

	Ⅰ组 (n=8) $\bar{X}\pm SD$	Ⅱ组 (n=8) $\bar{X}\pm SD$	Ⅲ组 (n=8) $\bar{X}\pm SD$	Ⅳ组 (n=6) 组 $\bar{X}\pm SD$
骨密度 g/cm^2	0.403±0.006	0.384±0.007△	0.363±0.012*	0.351±0.18**
抗弯强度 牛顿/mm^2	64.03±10.55	59.93±7.71△	42.72±4.33*	37.79±3.47**
骨小梁容积 %	43.17±5.69	35.01±5.77△	24.80±4.30*	17.33±5.12**

△：与Ⅰ组比较，差异无统计学意义 ($P>0.05$)；*：与Ⅰ组比较，差异有统计学意义 ($P<0.05$)；**：与Ⅰ组比较，差异有显著统计不学意义 ($P<0.01$)

参考文献

1. Kalu DN, et al. The aged rat model of ovarian hormone deficiency bone loss. Endocrinol 1989; 124 (1): 7.
2. 顾增发，等．用切除卵巢大鼠建立骨质疏松症模型的研究．中华老年医学杂志 1989; 8 (2): 118.
3. Oritoft G, et al. Reduced strength of rat cortical bone after glucocorticoid treatment. Calcif Tissue Int 1988; 43 (2): 376.
4. Martin RB, et al. Bone marrow fat content in relation to bone remodling and serum chemistry in intact and ovariectomized dogs. Calcif Tissue Int 1990; 46 (3): 327.
5. Lowe C, et al. Serum blocks the osteolytic effect of cortiol in neonatal mouse calvaria. Calcif Tissue Int 1992; 50 (2): 189.
6. Olgaaard K, et al. Glucocorticoid－induced osteoporosis in the lumbar spine, forearm and mandible of nephrotic patient: A double－blind study ofthe high－dosage, long－term effects of prednisone versus deflazacort. Calcif Tissue Int 1992; 50 (6): 490.
7. 刘忠厚主编．骨质疏松症防治与研究．第 1 版．北京：北京化学工业出版社，1994: 121～123.
8. 彭国瑞，等．不同剂量糖皮质激素所致"阳虚"动物模型的研究．中医杂志 1984; (4): 74.

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Abstract of Original Articles

The Evaluation of Operation and Conservative Therapy on the Transient Contusion of Cervical Spinal Cord *Fu Qin, Du Shixin, Zhang Yunqi, et al. The Second Clinical Institute, China Medical University, Shenyang* (110003)

The operation indication of the transient contusion of the cervical spinal cord has still not been very clear. Nine cases in total were studied. Among them, there were 3 cases treated with operation and the others with conservative therapy. The observation with Frankle evaluation had been followed up for 6－24 months. The results indicated that the spinal cord function of 3 cases in the conservative therapy group had been recovered basically to normal, and the function of hand in the operation group improved better than that in the former. It was suggested that the patients suffered from transient contusion, due to the injury of cervical spinal cord, should be treated, at first, with non－operative methods for 1－2 weeds; if the nervous function was not improved very well in this period, the operation should be applied as soon as possible, in order to recover the function of hand.

Key words Injury of spinal cord Cervical vertebra MRI

(Original article on page 3)

Complications following Treatment of Fracture with Orthofix Frame *Zhang Kaifang, Wang Kunzheng, Liu Anqing, et al. The Second Teaching Hospital, Xian Medical University* (710004)

126 cases of limbs' fracture had been treated with Orthofix Frame since 1993, and bony union have been achieved in 124 cases. The complications induced by this kind of frame fixation are summarized as pain, bleeding and effusion from pin tract, injury of nerve, swelling at the distal part of limbs, retranslocation and refracture, delayed union, nonunion, and infection at pin tract, etc. The cause, prevention and treatment of such complications are discussed.

Key words Orthofix frame fixation Complication Prevention and treatment

(Original article on page 6)

Experimental Research on the Establishment of Osteoporosis Model in Pregeriatic Rat with Glucocorticoid *Chen Dongyu, Shen Peizhi, Shi Yinyu, et al. Hospital of Shanghai Bao－Steel Metal Constructive Cooperation* (200941)

Owing to the effect of glucocorticoid, promoting bone substance absorption, the male pregeriatic SD rats had been injected intramuscularly with dexamethasone in different dosages (0. 05, 0. 1, 0. 4mg/100g BW), and thereafter, the changes in bone density of whole body, volume of bone trabeculae, and intensity of anticurvation were observed. The experimental results demonstrated that all of these parameters are decreased significantly in middle dosage group ($P<0.05$); those parameters in low dosage group tend to decrease but without statistical significance ($P>0.05$). It is considered that the osteoporosis model in pregeriatic rats could be established by intramuscular injection of dexamethasone, in the dose of 0. 25mg/100gBW, twice weekly, for 6 weeds.

Key words Glucocorticoid Osteoporosis Pathologic model

(Original article on page 8)

The Therapeutic Effect of Spinal Cord No. II on the Injury of Spinal Cord in Rats－Electrophysiological Study *Liu weidong, Han Fengyue. Institute of Orthopaedics and Traumatology, China Academy of TCM, Beijing* (100700)

The models of right hemi-transection of 12th thoracic spinal cord of 18 Wistar rats had been made and randomly divided into three groups. They were treated with Chinese herbs "Spinal Cord No. II", hydrocortisone, or normal saline respectively. The behavior changes of these experimental rats were observed daily, and the evoked electropotentials of the motion and the sensation were measured with electrophysiological methods for the evaluation of the function recovery after four weeks. It was discovered that there was good therapeutic effect of Spinal Cord NO. II, which was superior to that of hydrocorticoid in some extent.

Key words Injury of spinal cord Evoked electric