傲骨胶囊对去卵巢大鼠骨质疏松相关检测指标的影响

李学朋

(山东中医药大学,山东　济南　250014)

摘　要　目的:观察傲骨胶囊对去卵巢大鼠骨质疏松相关检测指标的影响。**方法:**将 50 只健康 10 周龄雌性 SD 大鼠分为 5 组,A 组 9 只,B 组 10 只,C 组 10 只,D 组 11 只,E 组 10 只。A 组大鼠切除卵巢周围部分脂肪,其余 4 组切除卵巢制成骨质疏松模型。从造模后第 11 天开始,C 组、D 组、E 组大鼠分别按 0.337 5 g·kg^{-1}、0.675 g·kg^{-1}、2.025 g·kg^{-1}以傲骨胶囊灌胃,A 组和 B 组按 10 mL·kg^{-1}以去离子水灌胃,每天 1 次,共 13 周,第 13 周末处死大鼠。从药物干预开始至处死前,每周测定 1 次各组大鼠的体质量。取各组大鼠左侧股骨,测定其股骨中点、远端和近端骨密度。取各组大鼠右侧股骨,测定其骨钙含量和骨恒重。**结果:**①体质量。药物干预前 5 组大鼠体质量比较,差异有统计学意义($F=7.230$,$P=0.000$)。组间两两比较:A 组大鼠体质量[(241.40±19.10) g]小于 B 组[(281.90±21.00) g]、C 组[(280.70±22.60) g]、D 组[(282.20±20.90) g]和 E 组[(281.70±23.40) g],差异均有统计学意义($P=0.000$,$P=0.000$,$P=0.000$,$P=0.000$)。药物干预 13 周后 5 组大鼠体质量均有增加($t=4.180$,$P=0.000$;$t=15.390$,$P=0.000$;$t=12.140$,$P=0.000$;$t=15.590$,$P=0.000$;$t=11.630$,$P=0.000$),对增加值进行组间比较,差异有统计学意义($F=7.364$,$P=0.000$)。进一步组间两两比较:A 组增加值[(100.20±39.25) g]小于 B 组[(178.10±36.78) g]和 D 组[(143.10±29.18) g],差异均有统计学意义($P=0.000$,$P=0.008$);B 组增加值大于 C 组[(116.20±30.43) g]、D 组和 E 组[(130.30±35.63) g],差异均有统计学意义($P=0.000$,$P=0.028$,$P=0.003$)。其余各组间两两比较,差异无统计学意义($P>0.05$)。②骨密度。5 组大鼠股骨远端、股骨中心点及股骨近端骨密度组间比较,差异均有统计学意义($F=15.549$,$P=0.000$;$F=4.688$,$P=0.005$;$F=4.343$,$P=0.005$)。B 组股骨远端、股骨中心点及股骨近端骨密度[(0.21±0.02) g·cm^{-2},(0.13±0.02) g·cm^{-2},(0.18±0.03) g·cm^{-2}]均低于 A 组[(0.27±0.02) g·cm^{-2},(0.16±0.01) g·cm^{-2},(0.22±0.02) g·cm^{-2}]、D 组[(0.26±0.02) g·cm^{-2},(0.16±0.03) g·cm^{-2},(0.20±0.02) g·cm^{-2}]、E 组[(0.26±0.03) g·cm^{-2},(0.18±0.01) g·cm^{-2},(0.21±0.01) g·cm^{-2}],差异均有统计学意义($P=0.000$,$P=0.001$,$P=0.000$;$P=0.000$,$P=0.001$,$P=0.039$;$P=0.000$,$P=0.000$,$P=0.003$);C 组股骨远端和股骨近端骨密度[(0.22±0.01) g·cm^{-2},(0.18±0.02) g·cm^{-2}]低于 D 组,差异均有统计学意义($P=0.000$,$P=0.039$);C 组股骨远端、股骨中心点[(0.15±0.02) g·cm^{-2}]及股骨近端骨密度均低于 E 组($P=0.000$,$P=0.001$,$P=0.003$);D 组股骨中心点骨密度低于 E 组($P=0.027$);其余各组间比较,差异均无统计学意义($P>0.05$)。③骨钙含量。5 组大鼠骨钙含量比较,差异有统计学意义($F=5.929$,$P=0.001$)。A 组骨钙含量[(254.12±19.11) mg·g^{-1}]大于 B 组[(203.23±30.58) mg·g^{-1}]和 C 组[(226.35±26.71) mg·g^{-1}],差异均有统计学意义($P=0.000$,$P=0.027$);B 组骨钙含量小于 D 组[(245.80±16.43) mg·g^{-1}]和 E 组[(239.40±37.30) mg·g^{-1}],差异均有统计学意义($P=0.001$,$P=0.005$);其余各组间比较,差异均无统计学意义($P>0.05$)。④骨恒重。5 组大鼠骨恒重比较,差异有统计学意义($F=5.147$,$P=0.001$)。E 组大鼠骨恒重[(664.51±44.75) mg]大于 A 组[(603.77±70.05) mg]、B 组[(603.38±36.57) mg]和 C 组[(611.93±53.03) mg],差异均有统计学意义($P=0.013$,$P=0.012$,$P=0.030$);其余各组间比较,差异均无统计学意义($P>0.05$)。**结论:**中、高剂量的傲骨胶囊能促进去卵巢大鼠对钙的吸收和利用,增加骨密度,具有明显的抗骨质疏松作用。同时傲骨胶囊还有抑制由雌激素水平降低所引起的体质量增加的作用。

关键词　骨质疏松　卵巢切除术　骨密度　傲骨胶囊　动物实验

Effect of AOGU CAPSULE on the detection indicators related to the osteoporosis of ovariectomized rats

*LI Xue-peng**. **Shandong University of Traditional Chinese Medicine*, *Jinan* 250014, *Shandong*, *China*

ABSTRACT　Objective: To observe the effect of AOGU CAPSULE on the detection indicators related to the osteoporosis of ovariectomized rats. **Methods**: Fifty healthy female SD rats of 10 weeks old were divided into 5 groups, 9 cases in group A, 10 cases in group B, 10 cases in group C, 11 cases in group D and 10 cases in group E. Rats in group A were administrated with fat removal around the ovary, while the others in the rest 4 groups were administrated with ovariectomy to build models of osteoporosis. Ten days after molding, the rats in group C, D and E were intragastric administrated with AOGU CAPSULE (0.3375 g/kg, 0.675 g/kg and 2.025 g/kg, respectively), while the others in group A and group B were intragastric administrated with deionized water (10 mL/kg), once per day for consecutive 13 weeks. All the

rats were executed at the end of the 13th week. During the period from the beginning of medicine intervention to execution, the body mass of rats of each group were measured once a week. The bone mineral density (BMD) were measured on the midpoint, distal end and proximal end of the left femur of the rats, and the bone calcium content (BCC) and bone constant weight (BCW) were measured on the right femur of the rats. **Results**: ①Body mass: there was statistical difference in body mass among the 5 groups before medicine intervention ($F = 7.230$, $P = 0.000$). As the results of further pairwise comparison showed, body mass of rats in group A ((241.40 ± 19.10) g) were lower than that of group B ((281.90 ± 21.00) g), C ((280.70 ± 22.60) g), D ((282.20 ± 20.90) g) and E ((281.70 ± 23.40) g) respectively, and there were statistical differences between them ($P = 0.000$, $P = 0.000$, $P = 0.000$, $P = 0.000$). Body mass of rats in the 5 groups were all increased 13 weeks after medicine intervention ($t = 4.180$, $P = 0.000$; $t = 15.390$, $P = 0.000$; $t = 12.140$, $P = 0.000$; $t = 15.590$, $P = 0.000$; $t = 11.630$, $P = 0.000$), and there was statistical difference in the increase value among the 5 groups ($F = 7.364$, $P = 0.000$). As the results of further pairwise comparison showed, the increase value of group A ((100.20 ± 39.25) g) was lower than that of group B ((178.10 ± 36.78) g) and group D ((143.10 ± 29.18) g) respectively, and there were statistical differences between them ($P = 0.000$, $P = 0.008$); the increase value of group B was larger than that of group C ((116.20 ± 30.43) g), D and E ((130.30 ± 35.63) g) respectively, and there were statistical differences between them ($P = 0.000$, $P = 0.028$, $P = 0.003$). There was no statistical difference between any couple of the rest groups ($P > 0.05$). ②BMD: there were statistical differences in BMD on distal femur, femoral midpoint and proximal femur among the 5 groups ($F = 15.549$, $P = 0.000$; $F = 4.688$, $P = 0.005$; $F = 4.343$, $P = 0.005$). BMD on distal femur, femoral midpoint and proximal femur of rats in group B ((0.21 ± 0.02) g/cm(2), (0.13 ± 0.02) g/cm(2), (0.18 ± 0.03) g/cm(2)) were all lower than those of group A ((0.27 ± 0.02) g/cm(2), (0.16 ± 0.01) g/cm(2), (0.22 ± 0.02) g/cm(2)), D ((0.26 ± 0.02) g/cm(2), (0.16 ± 0.03) g/cm(2), (0.20 ± 0.02) g/cm(2)) and E ((0.26 ± 0.03) g/cm(2), (0.18 ± 0.01) g/cm(2), (0.21 ± 0.01) g/cm(2)) respectively, and there were statistical differences between them ($P = 0.000$, $P = 0.001$, $P = 0.000$; $P = 0.000$, $P = 0.001$, $P = 0.039$; $P = 0.000$, $P = 0.000$, $P = 0.003$); BMD on distal and proximal femurs of rats in group C ((0.22 ± 0.01) g/cm(2), (0.18 ± 0.02) g/cm(2)) were all lower than those of group D, and there were statistical differences between them ($P = 0.000$, $P = 0.039$); BMD on distal femur, femoral midpoint ((0.15 ± 0.02) g/cm(2)) and proximal femur of rats in group D were all lower than those of group E respectively ($P = 0.000$, $P = 0.001$, $P = 0.003$); BMD on femoral midpoint of group D was lower than that of group E ($P = 0.027$); while there were no statistical differences between any couple of the rest groups ($P > 0.05$). ③BCC: there was statistical difference in BCC among the 5 groups ($F = 5.929$, $P = 0.001$). BCC of group A ((254.12 ± 19.11) mg/g) was larger than that of group B ((203.23 ± 30.58) mg/g) and group C ((226.35 ± 26.71) mg/g) respectively, and there were statistical differences between them ($P = 0.000$, $P = 0.027$); BCC of group B was lower than that of group D ((245.80 ± 16.43) mg/g) and group E ((239.40 ± 37.30) mg/g) respectively, and there were statistical differences between them ($P = 0.001$, $P = 0.005$); while there were no statistical differences between any couple of the rest groups ($P > 0.05$). ④BCW: there was statistical difference in BCW among the 5 groups ($F = 5.147$, $P = 0.001$). BCW of group E ((664.51 ± 44.75) mg) was larger than that of group A ((603.77 ± 70.05) mg), B ((603.38 ± 36.57) mg) and C ((611.93 ± 53.03) mg) respectively, and there were statistical differences between them ($P = 0.013$, $P = 0.012$, $P = 0.030$); while there were no statistical differences between any couple of the rest groups ($P > 0.05$). **Conclusion**: AOGU CAPSULE of medium and high dosage can promote the absorption and use of the calcium and increase BMD in ovariectomized rats, so it has significant antagonistic effect on osteoporosis. Meanwhile, AOGU CAPSULE also has the effect of inhibiting the increase of body mass caused by the lower level of estrogen.

Key words　Osteoporosis; Ovariectomy; Bone density; AOGU CAPSULE; Animal experimentation

随着人口老龄化的发展，骨质疏松症目前已成为一种严重危害老年人健康的疾病。傲骨胶囊是治疗骨质疏松症的中药制剂，我们通过实验观察了它对去卵巢大鼠骨质疏松相关检测指标的影响，现总结报告如下。

1　材料与仪器

1.1　实验动物　SPF 级健康 10 周龄雌性 SD 大鼠 50 只，体质量 250 ~ 300 g，由北京大学医学部实验动物科学部提供，实验动物合格证号：SCXK(京)2006-0008。

1.2　实验药物　傲骨胶囊，由泰安大凡神农制药有限公司提供，批号：20070716。

1.3　实验仪器　XR36 型双能 X 线吸收骨密度仪(美国 NORLAND 公司生产)；PE-5100 型原子吸收分光光度计(美国 PE 公司生产)。

2　方　法

2.1　分组及造模　适应性饲养 1 周后，将 50 只大鼠

随机分为 5 组，A 组 9 只，B 组 10 只，C 组 10 只，D 组 11 只，E 组 10 只。给所有大鼠按 40 mg · kg^{-1}腹腔注射 1% 戊巴比妥钠溶液进行麻醉，麻醉起效后 A 组大鼠经背部肋脊角切口切除卵巢周围部分脂肪，其余 4 组经背部肋脊角切口切除卵巢，最后分层缝合切口。

2.2 药物干预 造模后各组大鼠自由摄食，饮去离子水。从造模后第 11 天开始，C 组、D 组、E 组分别按 0.337 5 g · kg^{-1}、0.675 g · kg^{-1}、2.025 g · kg^{-1}以傲骨胶囊灌胃，A 组和 B 组按 10 mL · kg^{-1}以去离子水灌胃，每天 1 次，共 13 周。药物干预结束后处死大鼠，剥离双侧股骨，剔除周围附着的软组织后备用。

2.3 实验指标测定

2.3.1 体质量 从药物干预开始至处死，每周测定 1 次各组大鼠的体质量。

2.3.2 骨密度 以双能 X 线吸收骨密度仪分别测定左侧股骨中点、远端和近端骨密度。

2.3.3 骨钙含量和骨恒重 取大鼠右侧股骨在 105 ℃烘箱中烘干至恒重后（间隔 1 h 称量差值不超过 0.000 3 g）测量其质量，并用原子吸收法测定其骨钙含量。

2.4 统计学方法 采用 SPSS13.0 软件对所得数据进行统计分析，5 组大鼠体质量、骨密度、骨钙含量及骨恒重的组间比较采用方差分析，组间进一步两两比较采用 LSD-t 检验，检验水准 $\alpha = 0.05$。

3 结 果

3.1 体质量 药物干预前 5 组大鼠体质量比较，差异有统计学意义。组间两两比较：A 组大鼠体质量小于 B 组、C 组、D 组和 E 组（$P = 0.000$，$P = 0.000$，$P = 0.000$，$P = 0.000$）。5 组大鼠经 13 周药物干预后体质量均有增加，对增加值进行组间比较，差异有统计学意义。进一步组间两两比较：A 组增加值小于 B 组和 D 组（$P = 0.000$，$P = 0.008$）；B 组增加值大于 C 组、D 组和 E 组（$P = 0.000$，$P = 0.028$，$P = 0.003$）。其余各组间两两比较，差异无统计学意义（$P > 0.05$）。（表 1）

表 1 5 组大鼠体质量比较 g

组别	药物干预前	药物干预 13 周末	差值	t 值	P 值
A 组	241.40 ± 19.10	341.60 ± 52.60	100.20 ± 39.25	4.180	0.000
B 组	281.90 ± 21.00	460.00 ± 49.70	178.10 ± 36.78	15.390	0.000
C 组	280.70 ± 22.60	396.90 ± 39.00	116.20 ± 30.43	12.140	0.000
D 组	282.20 ± 20.90	425.30 ± 34.60	143.10 ± 29.18	15.590	0.000
E 组	281.70 ± 23.40	412.00 ± 42.00	130.30 ± 35.63	11.630	0.000
F 值	7.230		7.364		
P 值	0.000		0.000		

3.2 骨密度 5 组大鼠股骨远端、股骨中心点及股骨近端骨密度组间比较，差异有统计学意义。B 组股骨远端、股骨中心点及股骨近端骨密度均低于 A 组（$P = 0.000$，$P = 0.001$，$P = 0.000$）、D 组（$P = 0.000$，$P = 0.001$，$P = 0.039$）、E 组（$P = 0.000$，$P = 0.000$，$P = 0.003$）；C 组股骨远端和股骨近端骨密度低于 D 组（$P = 0.000$，$P = 0.039$）；C 组股骨远端、股骨中心点及股骨近端骨密度均低于 E 组（$P = 0.000$，$P = 0.001$，$P = 0.003$）；D 组股骨中心点骨密度低于 E 组（$P = 0.027$）；其余各组间比较，差异均无统计学意义（$P > 0.05$）。（表 2）

3.3 骨钙含量 5 组大鼠骨钙含量比较，差异有统计学意义。A 组骨钙含量大于 B 组和 C 组（$P = 0.000$，$P = 0.027$）；B 组骨钙含量小于 D 组和 E 组（$P = 0.001$，$P = 0.005$）；其余各组间比较，差异均无统计学意义（$P > 0.05$）。（表 2）

3.4 骨恒重 5 组大鼠骨恒重比较，差异有统计学意义。E 组大鼠骨恒重大于 A 组、B 组和 C 组（$P = 0.013$，$P = 0.012$，$P = 0.030$）；其余各组间比较，差异均无统计学意义（$P > 0.05$）。（表 2）

4 讨 论

骨质疏松症以骨量减少和骨组织细微结构退化为特征，可导致骨脆性及骨折危险性增加。骨质疏松性骨折好发于椎体、股骨颈、股骨转子间、桡骨远端及肱骨近端[1]。利用去卵巢大鼠骨质疏松模型研究骨质疏松症已经被广泛应用[2]。雌性大鼠在卵巢切除后松质骨骨量减少，骨强度下降，某些部位骨丢失现象加快，这种特征与人正常绝经后高转换型骨质疏松发生的骨丢失现象类似[3]。成年大鼠骨重建周期为 30 ~ 40 d，为了得到更加准确的实验结果，本研究将傲骨胶囊的治疗时间定为 13 周。

表 2　5 组大鼠骨密度、骨钙含量及骨恒重比较

组别	骨密度(g·cm^{-2})			骨钙含量(mg·g^{-1})	骨恒重(mg)
	股骨远端	股骨中心点	股骨近端		
A 组	0.27±0.02	0.16±0.01	0.22±0.02	254.12±19.11	603.77±70.05
B 组	0.21±0.02	0.13±0.02	0.18±0.03	203.23±30.58	603.38±36.57
C 组	0.22±0.01	0.15±0.02	0.18±0.02	226.35±26.71	611.93±53.03
D 组	0.26±0.02	0.16±0.03	0.20±0.02	245.80±16.43	644.29±52.00
E 组	0.26±0.03	0.18±0.01	0.21±0.01	239.40±37.30	664.51±44.75
F 值	15.549	4.688	4.343	5.929	5.147
P 值	0.000	0.005	0.005	0.001	0.001

分析本实验的结果，我们可以看出：①傲骨胶囊可以抑制由雌激素水平降低所引起的体质量增加，这一作用与傲骨胶囊的剂量无关；②中、高剂量的傲骨胶囊能增加去卵巢大鼠的骨密度；③中、高剂量的傲骨胶囊可以促进去卵巢大鼠对钙的吸收和利用。

骨质疏松症属中医“骨痿”“骨痹”范畴。《内经》云：“肾者，主蛰，封藏之本，精之处也。”《医经精义》亦云：“肾藏精，精生髓，髓生骨，故骨者肾之所合也，髓者精之所生也，精足则髓足。髓在骨内，髓足则骨强。”根据“肾藏精，主骨生髓”的理论，中医对骨质疏松症的治疗主要以补肾中药为主。各种原因所致的肾虚是骨质疏松症的主要病因，该病属本虚标实证，本虚以肾为主，涉及肝阴、脾气及气血不足，标实多为瘀血[4-5]。傲骨胶囊药物组成包括狗脊、乌梢蛇、补骨脂、淫羊藿等。狗脊祛风湿、补肝肾、强腰膝；乌梢蛇祛风除湿、通络止痉；补骨脂补肾壮阳、固精纳气；淫羊藿补肾壮阳、强筋骨、祛风湿。诸药合用，可起到补肾养血、填精益髓的作用。

现代药理学研究表明，补肾药物中含有类雌二醇样物质[6]，可显著提高雌性大鼠体内的雌激素水平。同时，淫羊藿、补骨脂等补肾中药所含的黄酮类物质，与己烯雌酚有类似的结构，具有雌激素样作用[7]，可以促进成骨细胞分化和增殖[8]。淫羊藿苷具有抑制体外培养破骨细胞和促进其凋亡的作用[9]。

综上所述，中、高剂量的傲骨胶囊能促进去卵巢大鼠对钙的吸收和利用，增加骨密度，具有明显的抗骨质疏松作用。同时傲骨胶囊还有抑制由雌激素水平降低所引起的体质量增加的作用。

5　参考文献

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