doi: 10.13241/j.cnki.pmb.2015.02.030

Evaluation of the Intervention Effect in Patients of Hyperthyroidism with Low Bone Mass after ^{131}I Treatment

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ABSTRACT Objective: To investigate the effect of intervention therapy in patients of hyperthyroidism with low bone mass after ^{131}I treatment. **Methods:** 100 cases of hyperthyroidism patients with low bone mass, were randomly divided into two groups: 50 cases in group A, taking Caltrate D and Rocaltrol after ^{131}I treatment; 50 cases in group B, bone natural recovery after ^{131}I treatment. Another 30 cases in group C as normal control group. Before ^{131}I treatment and after 3, 6 and 12 months, groups A and B were measured to observe the changes of bone mineral density (BMD) and evaluate the effect of intervention therapy. **Results:** (1) Group A: the BMD increased gradually and had a regular change. The lumbar vertebra (L2-4) reached to the level which there was no significant difference compared with that of group C after 12 months treatment (P=0.202>0.05). (2) Group B: the L2-4 had little decrease 3 months later, but increased evidently after 12 months (femoral neck: P=0.043; L2-4: P=0.000).(3) The changing extent of the L2-4 of these two groups appeared significant difference after 6 months (t= -2.416, P=0.018) and the disparity was more evident after 12 months (t= -3.259, P=0.002). **Conclusions:** The recovery time and curative effect of using ^{131}I combined with Caltrate D and Rocaltrol is superior to using the single ^{131}I treatment. The combined cure can effectively prevent further decrease in bone mass and reduce the occurrence of osteoporosis.

Key words: Hyperthyroidism; ^{131}I; Bone mineral density

Chinese Library Classification(CLC): R817.8 Document code: A

Article ID:1673-6273(2015)02-316-05

Introduction

In recent years, the research between hyperthyroidism and bone metabolism were reported frequent. Some said the whole body bone mineral density of hyperthyroidism patients were taken on descending tendency[1]. Some others said hyperthyroidism itself is also an independent risk factor for the development of hip and vertebral fracture [2,3]. In a word, hyperthyroidism can lead to bone loss which the mechanism basically has been identified publicly [4,5]. But for the intervention therapy of hyperthyroidism patients with low bone mass, it is little both at home and abroad, and especially using the ^{131}I treatment hyperthyroidism. At current, there are more researches on the intervention therapy of hyperthyroidism patients with osteoporosis. So the low bone mass did not get enough attention from patients and doctors. This study aims at taking calcium carbonate and active vitamin D to the hyperthyroidism patients with low bone mass to compare the bone changes under the conditions of both intervention therapy and natural recovery and compared with the control group to observe the effect of intervention therapy. The report is as follows:

1 Materials and methods

1.1 Study objects

Choosing hyperthyroidism patients with low bone mass who come to our hospital for taking ^{131}I from June 2012 to October 2013.They were randomly divided into two groups: Group A contains 50 cases including male 15 cases and female 35 cases and their mean age was 39.32 ± 7.1years old with 20.33 ± 2.1 kg/m^2 of body mass index (BMI). Group B contains 50 cases including male 12 cases and female 38 cases and their mean age was 40.05 ± 6.6 years old with 20.92 ± 1.9 kg/m^2 of BMI. Group C with 50 cases were the normal group matched with group A and B in age, height and weight in the same period for the BMD examination All the people had not the related diseases which could cause secondary osteoporosis, such as hyperparathyroidism, stomach and duodenal ulcer, diabetes, etc. They also had no drug history of taking corticosteroids, sex hormone, or parathyroid hormone, etc.

1.2 Diagnostic standard

The diagnostic standard of low bone mass on the basis of 2003 ISCD official positions on the interpretation of classification criteria of bone mineral density made by WHO in 1994 [6].

1.3 Treatment methods

Group A was the drug group which took Caltrate D produced by Wyeth Pharmaceutical Co.Ltd and Rocaltrol produced by Luoche Pharmaceutical Co.Ltd in Shanghai.The prescription was that took the former (each tablet contains elements of calcium 600mg, vitamin D125IU) one tablet each time and two times a day and took the latter (each tablet contains vitamin $D_3$0.25 μg) one tablet each time and one time a day. All the patients in group A took drugs with boilling water under proper temperature and avoided lie-down in half an hour. The bone mass of group B was left natural recovery Two groups A and B were required to measure BMD respectively in before ^{131}I treatment and after 3, 6 and 12 months.

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(Received: 2014-06-20 Accepted:2014-07-15)

Three months later, all patients of hyperthyroidism were basically cured (including hypothyroidism) through measuring free thyroid hormone in serum.Hypothyroidism patients take Levothyroxine Sodium Tablets (served by Merck KGaA) as a replacement therapy and their specific dose were adjusted according to the thyroxine level.

1.4 Instruments

The type of DPX IQ of dual energy X-ray absorptiometry produced in the American Lunar company was adopt to make patients'bone mineral density measured.The unit of BMD values is g/cm^2. FT3, FT4, TSH were detected by automatic and electrochemical luminescence analyzer of Elecsys2010 produced in Roche company of Germany.

1.5 Statistical analysis

The quantitative materials of normal distribution showed with mean± standard deviation. Datas before and after treatment were compared using the paired t test. The changing extent of BMD in groups A and B were compared using D-value of before and after treatment to make group t test. The independent samples t test was used between the control group and other two groups. It had statistical significance when the result showed P<0.05.

Table 1 BMD changes of two groups before and after treatment (g/cm^2, $\bar{x}\pm s$)

	Femoral neck				L2-4			
	A	B	t	P	A	B	t	P
0 month	0.783± 0.11	0.813± 0.09	-0.823	0.413	1.078± 0.06	1.073± 0.05	1.660	0.100
3 month	0.808± 0.07	0.819± 0.10	-0.099	0.921	1.109± 0.07	1.069± 0.08	-0.851	0.397
t	-0.748	-0.711			-2.111	-1.305		
P	0.458	0.48			0.04	0.198		
6 month	0.821± 0.08	0.831± 0.08	-0.670	0.505	1.137± 0.06	1.103± 0.08	-2.416	0.018
t	-2.120	-1.203			-6.463	-1.766		
P	0.059	0.235			0.000	0.07		
12 month	0.838± 0.06	0.848± 0.09	-1.917	0.048	1.207± 0.11	1.152± 0.15	-3.259	0.002
t	-4.472	-2.327			-8.312	-2.725		
P	0.000	0.043			0.000	0.000		

Note:0 month means before ^{131}I treatment.

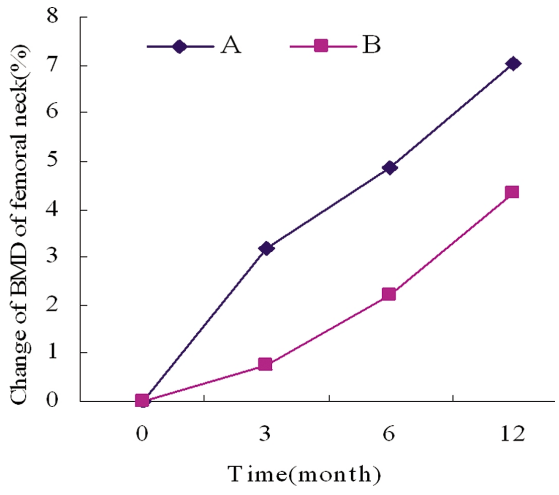

Fig. 1 Change of BMD of femoral neck

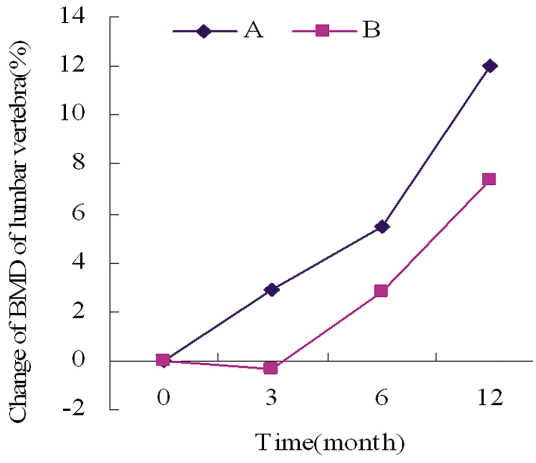

Fig. 2 Change of BMD of lumbar vertebra

2 Results

There were 4 cases of evident constipation symptoms during treatment occurred in group A. Without taking special treatment instead of urging them adhering to the medication, the symptoms got better gradually on their own.There was no fracture case occurs during treatment.

2.1 BMD analysis

(1) The changing extent of the L2-4 bone mineral density of these two groups appeared significant difference after 6 months and the disparity was more evident after 12 months (table 1). (2) Group A: The L2-4 increased significantly after 3 months and

reached to the level on which there was no significant difference compared with group C after 12 months treatment (table 1). The femoral neck and L2-4 increased gradually and have a regular change (Fig. 1 and Fig. 2). (3) Group B: the L2-4 had a little decreased 3 months later,but increased evidently after 12 months(Fig 2).

2.2 Comparison among group A, B and C

The BMD of group C in femoral neck and L2-4 are respectively 1.031± 0.09 g/cm^2 and 1.270 ± 0.09 g/cm^2. Compared with the above-mentioned two parts before ^{131}I treatment, after 3, 6 and 12 months, as for femoral neck, the T values of group A were respectively t= -7.272, -6.929, -5.721, -4.305, all the P values are 0.000; and group B were t= -9.360, -8.725, -6.474, -4.482, all the P values are also 0.000. As for L2-4, the T values of group A were t= -8.365, -6.439, -4.775, -2.290, P=0.000, 0.000, 0.000, 0.202. Itshowed that the L2-4BMD of group A reached to the level which was no significant difference with group C after 12 months treatment.The T values of group B were t= -10.504, -7.478, -5.705, -3.863, all the P values are also 0.000.

3 Discussion

Hyperthyroidism is a kind of self-immune disease which are resulted from a variety of thyroid hormone secretion.The annual incidence rate is about 0.2% ~0.3% [7]. It is one of important pathogenies caused secondary osteoporosis[8]. With the study going on, something were gradually discovered. On the bone mineral density screening of hyperthyroidism patients in our hospital for ^{131}I treatment, low bone mass and osteoporosis occurrence rate is respectively about 27.78% (100/360) and 9.72% (35/360) in 17 months. Even some research reported that the occurrence rate of hyperthyroidism patients with low bone mass as high as 30.2%[9]. In addition, it also was associated to the weak self-health care consciousness [10]. Therefore, the occurrence of bone loss induced by hyperthyroidism can not be ignored. If this part of the patients did not get timely and effective treatment, bone mass would further reduce and they would gradually developed into osteoporosis with high morbidity and mortality and the patient's quality of life would be influenced seriously.

Both one national and one international researches verified that the bone loss degrees of hyperthyroidism patients is relative to state of an illness [11]and the time of high dose of thyroid hormone incessantly action on the body is negative correlation with BMD[12]. However, course of disease is uncorrelated with bone loss in above two researches. Therefore, the symptoms of hyperthyroidism should be controlled firstly before making intervention therapy to the patients with low bone mass. ^{131}I could control the symptoms of hyperthyroidism in a short time and reduce the time of high dose of thyroid hormone incessantly action on skeletal and prevent the bone mass from further losing.At current, it is considered as a way which can cure the hyperthyroidism [13] In view of hyperthyroidism patients with low bone mass, calcium is the foundation [14]. After hydroxylation in liver and kidney, vitamin D_3 change into 1,25 (OH) 2 D_3 with stronger activity.The latter on one hand promote the absorption of small intestinal mucosa to the calcium.On the other hand, it can mobilize calcium in bone into the blood and help calcium deposite in bone and accelerate the bone formation process for improving bone mineral density. It is regarded as one of the indispensable drugs in the treatment of osteopenia and osteoporosis [15]. In addition,at home, Wang Jin-ping did the research firstly that the whole body BMD of hyperthyroidism patients is positive correlation with muscle mass [16]. Yet, the combination treatment of Caltrate D and Rocaltrol could strengthen the muscle to reduce the fall risk[17, 18] and the compliance and tolerability of treatments were good[19]. Therefor, it is essential and feasible to add Caltrate D and Rocaltrol to hyperthyroidism patients with low bone mass.

This study show that ^{131}I combined with Caltrate D and Rocaltrol in the treatment of hyperthyroidism with low bone mass lumbar vertebra BMD increased evidently 3 months later (P=0.04). They were unanimous about this.After three months treatment, the BMD of lumbar vertebra in group B was lower than before. The reasons might be as follows: for one thing, the level of thyroid hormone dropped so fast with ^{131}I treatment that the bone recovery were not stable.For another thing, lumbar vertebra was more sensitive to the decline of thyroid hormone and the specific mechanism was unclear. Therefore, this study suggested that it was better to supplement right amount calcium and active vitmin D after ^{131}I treatment in three months to buffer the effects of lumbar vertebra BMD caused by the sharply decline of thyroid hormone.There are different viewpoints about how long it will take when the bone mineral density reach the normal level after thyroid hormone recovery. It may be associated to the severity of the bone loss. The lumbar spine and femur BMD of hyperthyroidism with low bone mass after ^{131}I treatment 9~12 months increased not too many compared with before treatment[20]. This study showed that the BMD of two positions above-mentioned were improved to some extent after ^{131}I treatment 12 months but have not yet reached the normal level, while under the treatment of Caltrate D and Rocaltrol for 12 months after ^{131}I treatment, the BMD of lumbar vertebra reached the level which has no significant difference with the normal level. So, the supplement to some extent of Caltrate D and Rocaltrol in the early period after ^{131}I treatment is necessary.

The results show that ^{131}I combined with Caltrate D and Rocaltrol in the treatment of hyperthyroidism patients with low bone mass have evident effect. It could effectively prevent the bone mass from losing and reduce the occurrence of osteoporosis. Moreover, the combined cure was better than single treatment with ^{131}I in the recovery time and the curative effect. In addition, the price of two drugs are moderate and the suitable crowd are more extensive. They are worthy of clinical popularization. In addition,

this research still has many deficiencies. (1) The relatively small size of sample, especially the control group can not accurately reflect the normal level of bone mass. (2) The observation time is relatively short. Nothing was known about the prevention effect of fracture. (3) Despite the health education for 6 month were taken to the treatment group, there were still some uncontrollable factors to affect the compliance behavior. In a word, the above-mentioned problems need to be further researched and improved.

References

[1] Udayakumar N, Chandrasekaran M, Rasheed MH, et al.Evaluation of bone mineral density in throtoxicosis [J]. Singapore Med J, 2006, 47 (11): 947-950

[2] Vestergaard P, Rejnmark L, Mosekilde L. Influence of hyper-and hypothyroidism,and the effects of treatment with antithyroid drugs and levothyroxine on fracture risk [J]. Calcified Tissue International, 2005, 77: 139-144

[3] Ahmed LA, Schirmer H, Berntsen GK, et al. Self-reported diseases and the risk of non-vertebral fractures:the Tromso study [J]. Osteoporosis International, 2006, 17: 46-53

[4] Ma WJ, Yi QL, Yu MX. Research progress in the relationship between thyroid diseases and osteoporosis [J]. Fudan univ J Med Sci, 2012, 39 (4): 418-432

[5] Zhang Mei, Liu Chao (revised). Thyroid hormone and bone health [J]. Chinese Journal Osteoporosis, 2003, 9(2): 185-187

[6] Yang Hong-bin (translation), Qin Yue-juan (revised). The application of classification criteria made by WHO in 1994 were applied in a group of postmenopausal women other than Caucasian (interpretation to the 2005 ISCD official positions) [J]. Chinese Journal Osteoporosis, 2007, 13 (3): 208-216

[7] Wang Chun-mei, Wang Xue-mei. The development and current status of ^{131}I treatment for hyperthyroidism [J]. Int J Radiat Med Nucl Med, 2010, 34(1): 31-34

[8] Gogakos AI, Bassett JH, Williams GH, et al. Thyroid and bone [J]. Aroh Biochem Biophys, 2010, 503(1): 129 -136

[9] Xu Ying, Xu Xiao-hui. Clinical observation on bone mineral density and biochemical indexes of bone metabolism in patients with hyperthyroidism [J]. Labeled Immunoassays & Clin Med, 2004, 11 (2): 76-78

[10] Li Yan-ling, Liu Wei-hua, Bai Wei, et al. Observation of the intervention effect of perimenopausal women with osteopenia and osteoporosis in a community of Beijing [J]. Chin J Gen Pract, 2013, 12(7): 588-589

[11] Wang Ji-yan, Xing Xue-nong, Zhu Jie, et al. Correlative analysis of bone metabolism in patients with hyperthyroidism [J]. J of Radioimmunology, 2012, 25(3): 247-249

[12] EI Hadidy el HM, Ghonaim M, Gawad SSh, et al. Impact of severity, duration,and etiology of hyperthyroidism on bone turnover markers and bone mineral density in men[J]. BMC Endocr Disord, 2011,11:15

[13] Tan Jian. Interpretation of experts consensus on 131I therapy of Graves' hyperthyroidism[J]. Int J Endocrinol Metab, 2012, 32(2):73-75

[14] He Bin, Zhi Xi-mei, Zhang Wei-jie, et al. Study on preventive effect in quinquagenarian patients with bone loss of using calcium and Vitamin D[J]. Journal of Sun Yat-sen University(Medical Sciences), 2009, 30(3S): 193-195

[15] Rizzoli R, Boonen S, Brandi ML, et al. The role of calcium and vitamin D in the management of osteoporosis [J]. Bone, 2008, 42(2): 246-249

[16] Wang Jin-ping, Wang Ru-ying.The relationship between hyperthyroidism patients'bone mineral density and body component [J]. Chinese Remedies &Clinics, 2010, 10(6): 673-675

[17] Pfeifer M, Begerow B, Minne HW, et al. Effects of a short-term vitamin D and calcium supplementation on body sway and secondary hyperparathyroidism in elderly women [J]. Journal of Bone and Mineral Research, 2000, 15: 1113-1118

[18] Venning G. Recent developments in vitamin D deficiency and muscle weakness among elderly people[J]. BMJ, 2005, 330: 524-526

[19] Xia Wei-bo, Zhang Zhong-lan, Wang Hong-fu, et al. The efficacy and safety of calcitriol and/or Caltrate D in elderly Chinese women with low bone mass[J]. Acta Pharmacol Sin, 2009, 30(3): 372-378

[20] She Li-qun, Liao Guo-rong, Zou De-huan, et al. Clinical analysis of bone mineral density in patients of Graves' disease before and after ^{131}I therapy[J]. Chin J Osteoporos, 2004, 10(2): 215-220

甲亢低骨量患者 ^{131}I 治疗后干预治疗效果的评价

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摘要 目的:研究甲亢低骨量患者 131I 治疗后干预治疗的效果。**方法:**对 100 例甲亢低骨量患者,随机分为两组:A 组 50 例,^{131}I 治疗后口服钙尔奇 D 及罗盖全治疗;B 组 50 例,^{131}I 治疗后骨质自然恢复。另设 C 组 50 例为正常对照组。于 131I 治疗前、治疗后 3、6 及 12 个月测定 A、B 两组骨密度(BMD),观察其骨质变化并评价治疗效果。**结果:**(1)A 组随治疗时间延长 BMD 逐渐升高,具有一定的规律性,腰椎(L2-4)骨密度 3 个月提高明显(t= -2.111,P=0.04)且 12 个月时达到与 C 组无统计学差异(t= -2.290,P=0.202)。(2)B 组 3 个月时腰椎 BMD 有所降低,12 个月时升高明显(股骨颈 t= -2.327,P=0.043;腰椎(L2-4)t= -2.798,P=0.000)。(3)6 个月时两组腰椎骨密度改善幅度出现统计学差异(t= -2.416,P=0.018),12 个月时差异显著(t= -3.259,P=0.002)。**结论:**^{131}I 联合钙尔奇 D 与罗盖全治疗甲亢低骨量患者,其恢复时间及疗效均用 131I 治疗,能有效防止骨量的进一步下降及减少骨质疏松症的发生。

关键词: 甲状腺功能亢进症;^{131}I 量;骨密度

中图分类号:R817.8 **文献标识码:**A **文章编号:**1673-6273(2015)02-316-05

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(收稿日期:2014-06-20 接受日期:2014-07-15)