doi: 10.13241/j.cnki.pmb.2014.35.026

伊班膦酸钠联合钙尔奇D片治疗老年性骨质疏松症的疗效

郑 群 曹洪义 唐 毅 杨 婧 亢 君

（成都中医药大学附属成都市第五人民医院内分泌科 四川 成都 611130）

摘要 目的：探讨伊班膦酸钠注射液联合钙尔奇D片治疗老年性骨质疏松症的疗效及对患者血尿常规、肝肾功能及心电图的影响。**方法：**选择我院收治的72例老年骨质疏松症患者，采用随机数字表法将其分为观察组和对照组各36例，观察组给予伊班膦酸钠注射液联合钙尔奇D片进行治疗，对照组仅给予钙尔奇D片进行治疗，治疗时间为12个月，在治疗前，治疗后6个月及治疗后12个月时对比两组治疗效果及临床不良反应发生情况，并对两组患者的血尿常规、肝肾功能及心电图进行对比检查。**结果：**观察组在治疗6个月时BALP和TRAP-5b分别为（10.96± 0.93）ug/L、（3.71± 0.72）U/L，较治疗前和对照组均明显下降，比较差异均有统计学意义（P<0.05）；观察组在治疗12个月时BALP和TRAP-5b分别为（10.91± 0.81）ug/L、（3.73± 0.65）U/L，较治疗前和对照组亦显著下降，比较差异均有统计学意义（P<0.05）；对照组在治疗后6个月及12个月时，各检测指标统计值与治疗前比较，变化不大，比较差异均无统计学意义（P>0.05）；两种患者在治疗前、6个月、12个月时血尿常规、肝肾功能及心电图之间无统计学差异（P>0.05）；两组患者中均无明显严重的不良反应发生，不良反应发生情况比较差异无统计学意义（P>0.05）。**结论：**临床中联合应用伊班膦酸钠注射液和钙尔奇D片对老年性骨质疏松症进行治疗，可获得较为满意疗效，且对患者血尿常规、肝肾功能及心电图影响较小，不良反应发生率较低，病人耐受度较好，故值得在临床中应用。

关键词：伊班膦酸钠注射液；钙尔奇D片；老年性骨质疏松症；疗效

中图分类号：R68 **文献标识码：**A **文章编号：**1673-6273（2014）35-6897-03

Effects of Ibandronate Injection Combined with Caltrate D Tablets in the Treatment of Senile Osteoporosis

ZHENG Qun, CAO Hong-yi, TANG Yi, YANG Jing, KANG Jun

（Department of Endocrinology, The Chengdu Fifth People's Hospital Affiliated to Chengdu University of Traditional Chinese Medicine Chengdu, Sichuan, 611130, China）

ABSTRACT Objective: To investigate ibandronate injection combined with Caltrate D tablets in the treatment of senile osteoporosis efficacy and its influence on patients' urine routine, liver and kidney function and ECG. **Methods:** 72 elderly patients with osteoporosis admitted to hospital were randomly divided into the two- serial- method group and the control group, with 36 cases in each group, the observation group was given ibandronate injection combined with Caltrate D slices treatment, while the control group was given Caltrate D tablets for treatment, and the treatment period was 12 months. At time of before treatment, 6 -month and 12 -month post treatment, the therapeutic effect and clinical adverse reaction were compared, and the urine routine, liver and kidney function and ECG of the two groups of patients were also compared. **Results:** The BALP and TRAP-5b in study group 6 months post treatment were (10.96± 0.93) ug/L, (3.71± 0.72) U/L respectively, compared with before the treatment and the control groups, significant decrease was observed (P<0.05); observation group, in the 12th month of treatment, BALP and TRAP-5b were (10.91± 0.81) ug/L and (3.73± 0.65) U/L respectively, there was also significantly decrease when compared with before treatment and control group, and the difference was statistically significant (P<0.05); after 6 months of treatment and 12 months, no statistical difference on the value of each detection or treatment index was found in the control group during the treatment period (P>0.05); There was no urine routine, liver and kidney function and ECG -related statistically significant difference in two groups of patients before treatment, or after 6 months and 12 months of treatment, (P>0.05); patients in both groups had no significantly serious adverse events, and the incidence of adverse reactions was not significant (P>0.05). **Conclusion:** The combination of clinical ibandronate injections and Caltrate D tablets on senile osteoporosis treatment, obtains more satisfactory results and the urine routine, liver and kidney function and electrocardiogram were less affected. Since the incidence of adverse reactions was lower, and the patients could tolerate well, it is worth clinical application.

Key words: Ibandronate injection; Caltrate D film; Senile osteoporosis; Efficacy

Chinese Library Classification(CLC):R68 Document code: A

Article ID: 1673-6273(2014)35-6897-03

作者简介：郑群（1978-），女，本科，主治医师，从事内分泌科（骨代谢亚专业）方面的研究，E-mail:646698134@qq.com

（收稿日期：2014-05-21 接受日期：2014-06-16）

前言

近年来，对着人口老龄化的加速，老年人口骨质疏松症的发病率亦处于上升趋势，老年性骨质疏松症正逐渐成为我国乃至全世界所共同面临的健康问题[1,2]。骨质疏松症在临床中是指一种系统性骨病，其临床特征主要表现为骨量下降和骨微细结构遭到破坏，因而骨脆性增加，发生骨折危险性大大增加，往往受到轻微创伤或无外伤情况下亦较容易发生骨折。其是一种多因素所致的慢性疾病[3,4]。患者在骨折发生前，往往无特殊的临床表现。本研究旨在进一步论证伊班膦酸钠注射液联合钙尔奇 D 片对老年性骨质疏松症的疗效，现汇报如下。

1 资料与方法

1.1 一般资料

在本次研究中，受试的 70 例对象均来自于 2010 年 5 月 -2013 年 5 月我院收治的老年骨质疏松症患者，采用随机单盲的方式将其分为观察组和对照组各 35 例，其中观察组中男 26 例，女 9 例，年龄 65-81 岁，平均年龄（71.5± 5.1）岁，体重 65-78 kg，平均体重（68.5± 6.1）kg，平均腰椎 BMD 为（0.76± 0.12）g/cm^2，平均股骨颈 BMD 为（0.63± 0.11）g/cm^2，对照组中男 28 例，女 7 例，年龄 67-79 岁，平均年龄（69.3± 4.2）岁，体重 63-80kg，平均体重（67.1± 5.6）kg，平均腰椎 BMD 为（0.73± 0.11）g/cm^2，平均股骨颈 BMD 为（0.61± 0.12）g/cm^2，纳入标准参照：年龄均不小于 65 岁，腰椎（L3-L4）或总髋骨的密度（BMD）T 不大于 -2.5 个标准差，应用美国 Lunar 公司双能 X 线骨密度检测仪对患者 L1-L4 及股骨颈骨密度进行测定，结果均通过 T 值评分标准，自愿配合医护人员开展本次研究，并签署知情同意书。所有患者均排除其他代谢性骨病史，均排除应用过激素治疗的患者，排除严重心、肝、肾等疾病。所有患者均无自身免疫系统性疾病，均不伴有影响骨代谢的疾病等。两组患者在性别比，年龄，平均年龄，平均体重，平均腰椎、股骨颈 BMD 等一般资料方面比较差异无统计学意义（P>0.05），具有可比性。

1.2 方法

采用随机方式将患者分为观察组和对照组各 35 例，并将观察组和对照组患者中男、女分开住院，在分组后，给予对照组患者钙尔奇 D 片（苏州立达制药有限公司，卫药准字 X-83 号）口服治疗，1 片 / 日，每片含主要成份碳酸钙 1.5 克（相当于元素钙 600 毫克），维生素 D 125 国际单位。观察组在治疗开始后，每 3 个月给予患者伊班膦酸钠注射液进行治疗（配比为 2 mg 伊班膦酸钠（河北医科大学生物医学研制中心研制）加入 250 mL 生理盐水中溶解充分），每次经脉滴注时间在 2h 左右，同时按照对照组服用方法按时服用钙尔奇 D 片进行治疗，治疗总时间为 12 个月。

1.3 检测指标

在对患者进行治疗前、治疗 6 个月及治疗结束时的治疗效果及不良反应发生情况进行对比，主要的检测相关骨生化指标，主要指标包括抗酒石酸酸性磷酸酶 -5b（TRAP-5b）、骨源性碱性磷酸酶（BALP），对上述指标进行检测时应用方法为酶联免疫法（ELISA），同时对两组患者血尿常规、肝肾功能及心电图进行对比检查。

1.4 统计学方法

在本研究过程中，采用 SPSS 18.0 统计软件对数据进行处理，其中计量数据资料的整理应用均数± 标准差（$\bar{x}$± s）表示，并采用配对 t 检验的比较方法，计数资料及率的比较用 x^2 检验，P<0.05 表示差异具有统计学意义。

2 结果

2.1 两组患者治疗前后骨生化相关指标比较

经统计分析，两组在治疗前，BALP 和 TRAP-5b 水平含量比较差异无统计学意义（P>0.05），具有可比性。在治疗 6 个月时，观察组 BALP 和 TRAP-5b 分别为（10.96± 0.93）ug/L、（3.71± 0.72）U/L，较治疗前和对照组均明显下降，比较差异均有统计学意义（P<0.05）；在治疗 12 个月时，观察组 BALP 和 TRAP-5b 分别为（10.91± 0.81）ug/L、（3.73± 0.65）U/L，较治疗前和对照组亦显著下降，比较差异均有统计学意义（P<0.05）；对照组在治疗后 6 个月及 12 个月时，各检测指标统计值与治疗前比较，变化不大，比较差异均无统计学意义（P>0.05），详见表 1。

表 1 两组患者治疗前后骨生化相关指标比较（$\bar{x}$± s）

Table 1 Comparison of bone biochemical related indicators between two groups before and after treatment（$\bar{x}$± s）

组别 Groups	治疗前 Before treatment		6 个月 6 months		12 个月 12 months	
	BALP（μg/L）	TRAP-5b（U/L）	BALP（μg/L）	TRAP-5b（U/L）	BALP（μg/L）	TRAP-5b（U/L）
观察组(n=36) Observation group(n=36)	11.98± 0.71	5.33± 0.41	10.96± 0.93▲	3.71± 0.72▲	10.91± 0.81▲	3.73± 0.65▲
对照组(n=36) Control group(n=36)	12.01± 0.74	5.37± 0.46	11.97± 0.68	5.24± 0.35	12.02± 0.75	5.29± 0.38

注：与对照组和治疗前比较，▲P<0.05。

Note:Compared with control group and before treatment,▲P<0.05.

2.2 两组患者治疗前后血尿常规、肝肾功能及心电图比较情况

对患者在治疗前、6 个月、12 个月时行血尿常规、肝肾功能及心电图的相关检测，结果显示与治疗前比较，以上诸项指标的变化幅度不大，考虑临床检测中误差的存在，故认为治疗前

后患者诸上指标无明显变化,亦无统计学差异(P>0.05)。

2.3 两组不良反应发生比较情况

在治疗过程中,两组患者中均无明显严重的不良反应发生,观察组患者中仅有 1 例患者在静脉给予伊班膦酸钠注射液后出现轻微的低热、肌肉酸痛等不良反应,因患者反应轻微,故没有给予处理即自行恢复,患者耐受度较好。两组不良反应发生情况比较差异无统计学意义(P>0.05)。

3 讨论

临床中,老年性骨质疏松症是一种多发于老年人和绝经期后妇女的骨质疏松症[5,6]。随着年龄增加,机体内单位体积骨组织量会逐渐低于正常水平,骨小梁的间隙亦会增大,骨基质减少、骨量降低和骨强度降低,导致这些产生的病因往往是因机体内分泌紊乱、骨代谢失调及其他的废用因素等[7,8]。临床中,本病最常见的症状是腰痛,患者往往自述疼痛会沿脊柱向两侧扩散,于仰卧体位或坐位时疼痛减轻,直立或后伸体位时疼痛加剧,夜间、清晨疼痛加重,弯腰、肌肉运动、咳嗽和大便用力疼痛亦加重[9,10]。

对于老年骨质疏松治疗的主要方法是提倡预防和对症治疗[11,12]。对症治疗主要包括补钙和适当运动疗法,有时亦会联合应用中医学相关理论进行治疗,而预防性治疗措施主要包括:积极治疗能导致骨质疏松的内科病症;对于老年人而言,慎用糖皮质激素、肝素等;少吸烟、少饮酒等措施[13,14]。因钙是维持人体神经、骨骼系统、肌肉、细胞膜和毛细血管通透性正常功能的必需品,故维生素 D 能参与钙和磷的代谢,促进其吸收并对骨质形成有重要作用[15,16]。现今,临床中补钙常用的药物为钙尔奇 D 片,本品口服后吸收迅速而完全,药物主要分布于肝和脂肪组织,在肾、肝分别代谢为活性的骨化三醇。维生素 D3 及其代谢产物主要经胆道排泄,少量经肾排出[17,18]。伊班膦酸钠注射液为双膦酸盐类骨吸收抑制剂,其在体内主要通过与骨内羟磷灰石结合,抑制羟磷灰石的溶解和形成,进而产生抗骨吸收作用;临床中,其还可直接改变破骨细胞的形态学、直接抑制成骨细胞介导的细胞因子等起作用[19,20]。

通过本研究可以发现,观察组在治疗 6 个月和 12 个月时的 BALP 和 TRAP-5b 的水平变化不大,但较治疗前和对照组均明显下降,比较差异均有统计学意义(P<0.05),说明联合应用两种药物,可有效地维持骨生化指标在较低的范围,且观察组与对照组在治疗前、6 个月、12 个月时行血尿常规、肝肾功能及心电图的相关检测对比发现,检测结果与治疗前比较指标变化幅度不大、无明显变化,无统计学差异(P>0.05),说明临床中应用两种药物对患者本身无明显影响,且两组患者在治疗后均无明显严重的不良反应发生,不良反应发生情况治疗前后比较差异无统计学意义(P>0.05),亦说明患者对此次研究的两种药物的耐受性较好。综上所述,在临床中,联合应用伊班膦酸钠注射液和钙尔奇 D 片治疗老年性骨质疏松症,可获得较为满意的临床疗效,且对患者的血尿常规、肝肾功能及心电图的影响较小,不良反应发生率亦较低,病人耐受度较好,故值得在临床中联合推广应用。

参 考 文 献(References)

[1] Bianchi G, Czerwinski E, Kenwright A, et al. Long-term administration of quarterly IV ibandronate is effective and well tolerated in postmenopausal osteoporosis: 5-year data from the DIVA study long-term extension [J]. Osteoporosis international,2012,23(6): 1769-1778

[2] 刘雨.老年股骨颈骨折人工股骨头置换术 40 例护理体会[J]. 辽宁医学院学报,2010,31(5):466-467
Liu Yu. Nursing experience of 40 cases of femoral neck fracture with artificialfemoral head replacement [J]. Journal of Liaoning Medical University,2010,31(5):466-467

[3] Sieber P, Lardelli P, Kraenzlin C A, et al. Intravenous bisphosphonates for postmenopausal osteoporosis: Safety profiles of zoledronic acid and ibandronate in clinical practice [J]. Clinical drug investigation, 2013,33(2):117-122

[4] 杨敏,刘佳,范茂丹,等.唑来膦酸治疗原发性骨质疏松症的效果观察[J]. 现代生物医学进展,2013,7(3):533-535
Yang Min, Liu Jia, Fan Mao-dan, et al. zoledronic acid in the treatment of primary osteoporosis Observation [J]. Progress in Modern Biomedicine, 2013,7(3):533-535

[5] Miller P D, Ragi Eis S, Mautalen C, et al. Effects of intravenous ibandronate injection on renal function in women with postmenopausal osteoporosis at high risk for renal disease--the DIVINE study[J]. Bone,2011,49(6):1317-1322

[6] Vlak T, Kastelan D, Lozo P, et al. Monthly or weekly bisphosphonate? Evaluation of satisfaction in patients with postmenopausal osteoporosis using OPSAT-Q questionnaire during the BOOSTER study in Croatia[J]. Clinical rheumatology,2011,30(12):1549-1554

[7] Ziller V, Kostev K, Kyvernitakis I, et al. Persistence and compliance of medications used in the treatment of osteoporosis - Analysis using a large scale, representative, longitudinal German database [J]. International journal of clinical pharmacology and therapeutics, 2012,50(5):315-322

[8] Rizzoli R. Bisphosphonates for post-menopausal osteoporosis:are they all the same?[J]. QJM, 2011,104(4):281-300

[9] Jansen J P, Bergman G J, Huels J, et al. The efficacy of bisphosphonates in the prevention of vertebral, hip, and nonvertebral-nonhip fractures in osteoporosis: a network meta-analysis [J]. Seminars in Arthritis and Rheumatism, 2011,40(4): 275-284

[10] Xu Y, Viswanathan H N, Ward M A, et al. Patterns of osteoporosis treatment change and treatment discontinuation among commercial and Medicare Advantage Prescription Drug members in a national health plan [J]. Journal of evaluation in clinical practice,2013,19(1): 50-59

[11] Leif Mosekilde, Peter Vestergaard, Lars Rejnmark, et al. The pathogenesis, treatment and prevention of osteoporosis in men [J]. Drugs,2013,73(1):15-29

[12] 汪玉海,金丽娟,高俊,等.脂肪干细胞复合 PLGA 对骨质疏松骨折愈合后生物力学的影响[J]. 宁夏医科大学学报,2013,35(3):244-247

(下转第 6903 页)

参 考 文 献(References)

[1] House JW. Brackmann DE. Facial nerve grading systcm [J]. Otolaryngol Hcad Ncck Surg, 1985,93(2):146-147

[2] Samii M, Mattnies C. Management of 1000 vestibular schwannomas (acoustic neuromas):hearing function in 1000 tumir resections [J]. Neurosurgery, 1997,40 (2):248-262

[3] Matthics C, Samii M, Kerbs S. Management of vestibular schwannomas (acoustic neuromas): radiological features in 202 cases ? Their value for diagnosis and their predictive importance [J]. Neurosurgery,1997,40(3):469-482

[4] Tringali S, Charpiot A, Ould MB, et al. Characteristics of 629 vestibular schwannomas according to preoperative caloric responses [J]. Otol Neurotol, 2010,31(3):467-472

[5] Mehrotra N, Behari S, Pal L, et al. Giant vestibular schwannomas: focusing on the differences between the solid and the cystic variants [J]. Br J Neurosurg, 2008,22(4):550-556

[6] Mathieu D, Kondziolka D, Flickinger JC, et al. Stereotactic radiosurgery for vestibular schwannomas in patients with neurofibromatosis type 2: an analysis of tumor control, complications, and hearing preservation rates[J]. Neurosurgery, 2007,60(3):460-470

[7] Combs SE, Welzel T, Schulz-Ertner D, et al. Differences in clinical results after LINAC-based single-dose radiosurgery versus fractionated stereotactic radiotherapy for patients with vestibular schwannomas[J]. Int J Radiat Oncol Biol Phys, 2010,76(1):193-200

[8] Allen KP, Isaacson B, Kutz JW, et al. The association of meningitis with postoperative cerebrospinal fluid fistula [J]. J Neurol Surg B Skull Base, 2012,73(6):401-404

[9] Togashi S, Maruya J, Nerome C, et al. Contralateral hearing loss after acoustic neuroma surgery[J]. J Clin Neurosci, 2014,21(5):863-865

[10] Ahmed OH, Mahboubi H, Lahham S, et al. Trends in demographics, charges, and outcomes of patients undergoing excision of sporadic vestibular schwannoma [J]. Otolaryngol Head Neck Surg, 2014,150 (2):266-274

[11] Charabi S, Tos M, Borgesen SE, et al. Cystic acoustic neuromas results of translabrinthinc surgery [J]. Arch Otolaryngol Heck Surg, 1994,120(12):1333- 1338

[12] Benoudiba F, Toulgoat F, Sarrazin JL. The vestibulocochlear nerve (VIII)[J]. Diagn Interv Imaging, 2013,94(10):1043-1050

[13] Régis J, Carron R, Delsanti C, et al. Radiosurgery for vestibular schwannomas[J]. Neurosurg Clin N Am, 2013,24(4):521-530

[14] Mahboubi H, Ahmed OH, Yau AY, et al. Complications of surgery for sporadic vestibular schwannoma[J]. Otolaryngol Head Neck Surg, 2014,150(2):275-281

[15] Alotaibi NM, Makoshi Z, Orz Y. Recovery from deafness in the contralateral ear of surgery in NF 2 patient [J]. Can J Neurol Sci, 2013,40(5):754-756

[16] Ishak WS, Zhao F, Rajenderkumar D, et al. Measurement of subtle auditory deficit in tinnitus patients with normal audiometric thresholds using evoked otoacoustic emissions and threshold equalizing noise tests[J]. Int Tinnitus, 2013,18(1):35-44

[17] Rykaczewski B, Zabek M. A meta-analysis of treatment of vestibular schwannoma using Gamma Knife radiosurgery [J]. Contemp Oncol (Pozn), 2014,18(1):60-66

[18] Andaluz N, Van Loveren HR, Keller JT, et al. Anatomic and clinical study of the orbitopterional approach to anterior communicating artery aneurysms[J]. Neurosurgery, 2003,52(5):1140-1148

[19] Goddard JC, Oliver ER, Lambert PR, et al. Prevention of cerebrospinal fluid leak after translabyrinthine resection of vestibular schwannoma[J]. OtolNeurotol, 2010,31(3):473-477

[20] Kliesch S, Vogelgesang S, Benecke R, et al. Malignant brain oedema after radiosurgery of a medium-sized vestibular schwannoma[J]. Cent Eur Neurosurg, 2010,71(2):88-91

(上接第 6899 页)

Wang Yu-hai, Jin Li-juan, Gao Jun, et al. Effect of Adipose Derived Stem Cells in PLGA on Biomechanics after Osteoporotic Fracture-healing [J]. Journal of Ningxia Medical University,2013,35 (3):244-247

[13] 刘雄.阿伦膦酸钠治疗原发性骨质疏松症的 4 年临床研究[J]. 现代生物医学进展,2009,12(24):4722-4724

Liu Xiong. Clinical studies of alendronate treatment of primary osteoporosis four years [J]. Progress in Modern Biomedicine,2009,12 (24):4722 -4724

[14] Briot K, Cortet B, Thomas T, et al. 2012 update of French guidelines for the pharmacological treatment of postmenopausal osteoporosis[J]. Joint, bone, spine,2012,79(3):304-313

[15] Belaya Z E. Should we really compare absolute risk reduction in different trials on osteoporosis: comment on the article by Ringe JD and Doherty JG [J]. Rheumatology international,2011,31 (12): 1669-1671

[16] Yeh Y, Slovik D, Carter D, et al. Intravenous bisphosphonates for post-menopausal osteoporosis: adherence to a network guideline [J]. Journal of Clinical Pharmacy and Therapeutics,2011,36(3):342-347

[17] Wade S W, Satram Hoang S, Nadkar A, et al. Impact of medication adherence on health care utilization and productivity:self-reported data from a cohort of postmenopausal women on osteoporosis therapy [J]. Clinical therapeutics,2011,33(12):2006-2015

[18] Treeprasertsuk S, Silveira MG, Petz JL, et al. Parenteral bisphosphonates for osteoporosis in patients with primary biliary cirrhosis.[J]. American journal of therapeutics,2011,18(5):375-381

[19] Curtis J R, Safford M M. Management of osteoporosis among the elderly with other chronic medical conditions [J]. Drugs and aging, 2012,29(7):549-564

[20] Kun-Juan Zhang, Jian Zhang, Ze-Kun Kang, et al. Ibandronate for prevention and treatment of glucocorticoid-induced osteoporosis in rabbits[J]. Rheumatology international,2012,32(11):3405-3411