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唑来膦酸注射液联合骨肽注射液治疗绝经后骨质疏松症的临床疗效及安全性分析*

王 玲 张 新 白 云 周玉红 王世蓉

（锦州医科大学附属辽河油田总医院暨第四临床学院内分泌科 辽宁 盘锦 124010）

摘要 目的:研究唑来膦酸注射液联合骨肽注射液治疗绝经后骨质疏松症的临床效果以及安全性。**方法:**选择2014年1月～2018年1月我院收治的100例绝经后骨质疏松症患者,将其随机分为两组。对照组采用静脉滴注唑来膦酸注射液5 mg一次,观察组在对照组基础上静脉注射骨肽注射液,每次30 mg,每天1次。治疗6个月后,检测并比较两组治疗前后的骨代谢指标(血清骨特异性碱性磷酸酶(BAP)、甲状旁腺素(PTH)、血磷(P)、血钙(Ca)和碱性磷酸酶(ALP))以及骨转换指标(骨钙素(OC)和Ⅰ型胶原交联C-末端肽(CTX-1))的变化及不良反应的发生情况。**结果:**治疗后,观察组总有效率明显高于对照组(P<0.05);两组血清ALP、PTH以及BAP等骨代谢指标均较治疗前明显降低(P<0.05),且观察组以上指标明显低于对照组(P<0.05);两组的OC均较治疗前明显升高(P<0.05),CTX-1均较治疗前明显降低(P<0.05),且观察组的骨转换指标改善的程度较对照组更为明显(P<0.05)。观察组的不良反应发生率为8.00 %(4/50),明显低于对照组[18.00 %(9/50)](P<0.05)。**结论:**唑来膦酸注射液联合骨肽注射液治疗绝经后骨质疏松症的效果明显优于单独使用唑来膦酸注射液,其可以显著改善患者的骨代谢及骨转换状态,且安全性更高。

关键词:唑来膦酸注射液;骨肽注射液;骨质疏松症;疗效;安全性

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Clinical Efficacy and Safety of Zoledronic Acid Injection Combined with Bone Peptide Injection in the Treatment of Postmenopausal Osteoporosis*

WANG Ling, ZHANG Xin, BAI Yun, ZHOU Yu-hong, WANG Shi-rong

(Endocrinology department, Liaohe Oilfield General Hospital and fourth Clinical College Affiliated to Jinzhou Medical University, Panjin, Liaoning, 124010, China)

ABSTRACT Objective: To investigate the clinical efficacy and safety of zoledronic acid injection combined with bone peptide injection in the treatment of postmenopausal osteoporosis. **Methods:** 100 cases of patients with postmenopausal osteoporosis admitted to our hospital from January 2014 to January 2018 were randomly divided into two groups. The control group was given zoledronic acid injection 5 mg once, while the observation group was given bone peptide injection 30 mg once a day on the basis of the control group. After 6 months of treatment, the changes of bone metabolism indexes (serum bone specific alkaline phosphatase (BAP), parathyroid hormone (PTH), blood phosphorus (P), blood calcium (Ca) and alkaline phosphatase (ALP), bone turnover indexes (OC) and collagen type I cross-linked C-terminal peptide (CTX-1) and adverse reactions were detected and compared between the two groups before and after treatment. **Results:** After treatment, the total effective rate of observation group was significantly higher than that of the control group(P<0.05); the serum ALP, PTH and BAP of both groups were significantly lower than those before treatment(P<0.05), and the above indexes of observation group were significantly lower than those of the control group(P<0.05); the OC of the two groups were significantly higher than before treatment(P<0.05), the CTX-1 was significantly lower than before treatment(P<0.05). The improvement of bone turnover index in the observation group was more significant than that in the control group (P<0.05). The incidence of adverse reactions in the observation group was 8%(4/50), which was significantly lower than that in the control group [18.00% (9/50)] (P<0.05). **Conclusion:** Zoledronic acid injection combined with bone peptide injection is significantly effective than zoledronic acid injection alone in the treatment of postmenopausal osteoporosis, which can significantly improve bone metabolism and bone turnover with higher safety.

Key words: Zoledronic acid injection; Bone peptide injection; Osteoporosis; Efficacy; Safety

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前言

骨质疏松症是多种原因引起的一组全身性骨骼疾病,常见发病人群为绝经期女性以及中老年人[1-3],轻者会出现腰背痛,中度以上的骨质疏松症患者则会出现驼背、骨折、身高缩短、肺功能受损以及运动障碍等症状,严重者甚至能对其呼吸功能造

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作者简介:王玲(1970-),女,本科,副主任医师,研究方向:糖尿病、骨质疏松、甲状腺,电话:13050883233,E-mail:wangling_197003@163.com

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成影响,引发呼吸困难和胸闷等症状[4-7]。目前,临床上有多种抗骨质疏松症药物,其中,唑来膦酸钠是同类药物中具有抑制最强骨吸收效果的药物。研究表明唑来膦酸钠抑制骨吸收的强度是阿仑膦酸盐的 25~114 倍,是帕米磷酸盐的 100~850 倍[8]。骨肽能有效促进机体内骨细胞的生成,使骨钙沉积量大大增加,有效改善骨质疏松症患者的症状[9]。我院于 2014 年 1 月～2018 年 1 月采用唑来膦酸注射液联合骨肽注射液治疗绝经后骨质疏松症 50 例,取得了较好的临床效果,现将结果报道如下。

1 资料与方法

1.1 一般资料

选择 2014 年 1 月～2018 年 1 月我院收治的绝经后骨质疏松症患者 100 例,纳入标准:患者均出现显著的骨痛症状并伴有不同程度的日常生活功能受限,所有患者均签署知情同意书。排除标准:排除严重脊柱侧弯、骨软化症、Paget 疾病、肾性维生素 D 缺乏性佝偻病、甲状旁腺功能亢进症以及强直性脊柱炎等疾病患者。采取抽签法将 100 例绝经后骨质疏松症患者随机分为两组。观察组 50 例,年龄 53~87 岁,平均 (60.38± 9.32) 岁;病程 10 个月 ~11 年,平均(3.74± 1.65) 年;体重47~78 kg,平均(56.32± 11.52) kg;身高 151~172 cm,平均(159.41± 9.38) cm。对照组 50 例,年龄 54~88 岁,平均(60.23± 10.14) 岁;病程 10 个月 ~ 11 年,平均(3.92± 1.78) 年;体重 48~76 kg,平均(57.14± 12.38) kg;身高 152~171 cm,平均(160.23± 10.54) cm。两组的基线资料比较差异均无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

对照组:静脉滴注唑来膦酸注射液(国药准字 H20113138,生产厂家:江苏正大天晴药业股份有限公司,规格:100 mL: 5 mg) 5 mg 一次。

观察组:在对照组基础之上给予骨肽注射液 (国药准字 H50022108,生产厂家:重庆国泰康宁制药有限责任公司,规格:5 mL: 25 mg) 静脉注射,每次 30 mg,每天 1 次。治疗 15 d。6 个月后检测两组患者相关指标。

1.3 观察指标

疗效判断标准:① 显效:患者的骨痛症状基本消失;② 有效:患者的骨痛症状得到显著的改善;③ 无效:患者的骨痛症状无任何的改善。

骨代谢指标检测:使用南京颐兰贝生物科技有限公司的 ES-380 全自动生化分析仪对两组患者治疗前后的血清骨特异性碱性磷酸酶(BAP)、甲状旁腺素(PTH)、血磷(P)、血钙(Ca)和碱性磷酸酶(ALP)等骨代谢指标进行检测。

骨转换指标检测:所有患者均空腹采集 5 mL 上肢静脉血,采用放射免疫分析法检测骨钙素(OC)水平,采用酶联免疫法检测Ⅰ型胶原交联 C- 末端肽(CTX-1)水平。

1.4 统计学分析

采用 SPSS21.0 软件进行数据分析,计量资料(骨代谢水平和骨转换指标)以 $\bar{x}\pm s$ 表示,组间和组内对比分别用成组和配对 t 检验,计数资料(临床疗效和不良反应)组间比较采用 x^2 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组临床疗效对比

与对照组总有效率 (78.00%) 比较,观察组总有效率 (94.00%)明显升高(P<0.05)。

表 1 两组临床疗效比较[例(%)]

Table 1 Comparison of the clinical effect between two groups [n(%)]

Groups	n	Effective	Valid	Invalid	The total effect rate
Control group	50	18(36.00)	21(42.00)	11(22.00)	78.00
Observation group	50	21(42.00)	26(52.00)	3(6.00)	94.00 *

Note: Compared with the control group, *P<0.05.

2.2 两组治疗前后骨代谢水平对比

治疗后,两组血清骨代谢指标(ALP、PTH 和 BAP)均较治疗前明显降低(P<0.05),且观察组以上指标均明显低于对照组(P<0.05)。

表2 两组治疗前后骨代谢水平对比($\bar{x}\pm s$)

Table 2 Comparison of the bone metabolism level before and after treatment between two groups ($\bar{x}\pm s$)

Groups	n		ALP (U/L)	Ca (mmol/)	P (mmol/)	PTH (pmol/L)	BAP (U/L)
Control group	50	Before treatment	35.27 ± 12.64	2.17± 0.29	1.36± 0.34	1.48± 0.29	79.43± 17.63
		After treatment	31.58± 13.38#	2.21± 0.36	1.38± 0.39	1.35± 0.26#	72.24± 16.31#
Observation group	50	Before treatment	35.27± 11.14	2.19± 0.36	1.37± 0.31	1.47± 0.24	79.57± 16.82
		After treatment	26.35± 12.19*#	2.22± 0.37	1.35± 0.28	1.28± 0.19*#	65.14± 15.53*#

Note: compared with the control group, *P<0.05; compared with before treatment, #P<0.05.

2.3 两组治疗前后骨转换指标对比

治疗后,两组 OC 均较治疗前明显升高(P<0.05),CTX-1 均较治疗前明显降低 (P<0.05),且观察组 CTX-1 显著低于对照组,而 OC 明显高于对照组(P<0.05)。

2.4 两组不良反应发生情况的比较

观察组出现发热 2 例,肌痛 1 例,关节痛 1 例;对照组出现

发热9 例,肌痛 2 例,关节痛 2 例。观察组的不良反应发生率为 8.00%(4/50),明显低于对照组[26.00%(13/50)](P<0.05)。两组骨质疏松症患者经过对症治疗后不良反应症状均消失。

表 3 两组治疗前后骨转换指标对比($\bar{x}\pm s$)

Table 3 Comparison of the bone turnover markers between two groups before and after treatment($\bar{x}\pm s$)

Groups	n		CTX-1(ng/mL)	OC(ng/mL)
Control group	50	Before treatment	0.33± 0.08	5.25± 0.23
		After treatment	0.28± 0.06#	7.26± 0.48#
Observation group	50	Before treatment	0.34± 0.07	5.26± 0.17
		After treatment	0.20± 0.05*#	9.13± 0.52*#

Note: Compared with the control group, *P<0.05; compared with before treatment, #P<0.05.

3 讨论

骨质疏松症作为内分泌科常见的一种骨代谢疾病,会使患者的骨基质不断减少,骨密度降低,骨皮质变薄,对患者造成疼痛的同时,还极易引发骨折,严重困扰着很多绝经期女性和老年人,成为临床上研究的热点问题[10,11]。骨质疏松症的发病原因比较复杂,与运动、饮食习惯、日照时间、遗传以及性激素水平等多种因素有关,女性围绝经期是该病的危险因素之一[12-14]。由于骨质疏松症的成因复杂,临床上预防和治疗该病缺乏单一且有效的手段,主要采取联合用药综合治疗方案。临床上常常采用维生素和钙剂等联合使用,但效果往往并不满意。唑来膦酸可以通过特异性地作用于骨的二磷酸化合物,对由于破骨活性增加而造成的骨吸收进行明显的抑制,且唑来膦酸对矿化骨具有高度的亲和力,能选择性作用于骨骼[15-18]。有研究表明唑来膦酸注射液能使脊柱骨折率、骨折总发生率以及髋骨骨折率分别降低 70%、24%、40%[19]。

骨肽含有多肽类骨代谢因子、有机磷、无机钙、有机钙、无机盐、无机钙、氨基酸、微量元素以及多种骨骼生长所必需的生长因子,多种生长因子可参与人体骨代谢过程,促进骨骼的愈合及骨新生,临床常用来治疗骨折康复期,退行性骨关节病及骨代谢疾病等[20-24]。本研究将唑来膦酸注射液以及骨肽注射液联合使用,结果两种药物联合使用治疗绝经后骨质疏松症可以有效改善患者的临床症状。

CTX-1 可以特异性地反映 Ⅰ 型胶原的分解程度,而 Ⅰ 型胶原分解时所产生的末端肽和吡啶交联物又可以有效反映机体的骨吸收情况[25-27]。如果机体 CTX-1 的表达水平升高,则表明其骨量丢失情况加重,骨吸收速率加快。OC 水平的改变是由于成骨细胞活性发生变化引起,其可以特异而敏感地反映患者的骨代谢状态、成骨细胞活性和骨形成速率[28-30]。骨转化指标 CTX-1 以及 OC 能作为评估骨质疏松症患者治疗效果的有效指标。本研究结果显示唑来膦酸注射液联合骨肽注射液治疗后能有效抑制骨吸收,改善骨转换状态,并促进骨形成。可能与降低 CTX-1 水平而抑制骨吸收,且增加 OC 水平而促进骨形成,是其发挥治疗效果的重要作用机制。血骨特异性碱性磷酸酶、甲状旁腺素、血磷、血钙和碱性磷酸酶可以在一定程度上反映机体骨转化的过程。本研究结果显示观察组治疗后骨代谢水平(ALP、PTH 和 BAP)降低更为明显,表明唑来膦酸注射液以及骨肽注射液联合使用有助于改善绝经后骨质疏松症患者的血清相关骨代谢标志物水平。分析其原因为骨肽注射液可以有效抑制破骨细胞的骨吸收作用,并且能促进成骨细胞发生进一步的分化,调节机体的骨代谢状态,刺激成骨细胞发生增生,从而促进新骨的形成,并调节磷和钙的代谢,使骨钙沉积量明显增加,具有较强的镇痛、抗炎和防治骨质疏松效果,且长期用药并不会产生明显的毒副反应。以上结果均证实唑来膦酸注射液联合骨肽注射液是治疗绝经后骨质疏松症的安全有效方法,在改善患者的骨代谢及骨转换状态方面明显优于单一静脉滴注唑来膦酸注射液。

综上所述,唑来膦酸注射液联合骨肽注射液治疗绝经后骨质疏松症的效果明显优于单独使用唑来膦酸注射液,其可以显著改善患者的骨代谢及骨转换状态,且安全性更高。

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