

doi: 10.13241/j.cnki.pmb.2019.18.033

鲑鱼降钙素对胸腰椎脊柱骨折术后 I 型胶原氨基端延长肽、 I 型胶原 C 端肽 β 降解产物的作用 *

张中平¹ 赵毅¹ 曹华佗¹ 王飞² 杨明智^{1Δ}

(1 延安市人民医院,骨科一病区 陕西 延安 716000;2 延安大学附属医院 脊柱外科 陕西 延安 716000)

摘要 目的:探讨鲑鱼降钙素对胸腰椎脊柱骨折术后 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物的作用。**方法:**选择 2014 年 3 月至 2016 年 5 月我院收治的胸腰椎脊柱骨折患者 80 例,将其随机分为观察组和对照组,每组 40 例。两组均采用微创经皮椎弓根螺钉内固定术,对照组术后给予常规治疗,观察组术后给予鲑鱼降钙素治疗。比较两组患者治疗前后的骨密度、I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物、视觉模拟疼痛评分 (VAS) 评分、Oswestry 功能障碍指数评分 (ODI) 评分、Harris 评分的变化、骨折愈合时间及不良反应的发生情况。**结果:**治疗后,观察组患者骨密度及 Harris 评分明显高于对照组 ($P<0.05$), I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物、VAS 评分和 ODI 评分均低于对照组 ($P<0.05$); 观察组患者骨折愈合时间明显短于对照组 ($P<0.05$), 不良反应发生率 (7.50%) 较对照组 (10.00%) 比较无显著性差异 ($P>0.05$)。**结论:**鲑鱼降钙素用于胸腰椎脊柱骨折术后可有效改善患者骨密度, 促进骨折愈合且不会增加不良反应。

关键词:胸腰椎脊柱骨折; 鲑鱼降钙素; I 型胶原氨基端延长肽; I 型胶原 C 端肽 β 降解产物

中图分类号:R683 **文献标识码:**A **文章编号:**1673-6273(2019)18-3550-04

Effect of Calcitonin on the Amino Terminal Elongation Peptide of Type I Collagen and Type I Collagen C-Terminal Peptide β Degradation Products after Thoracolumbar Spine Fracture*

ZHANG Zhong-ping¹, ZHAO Yi¹, CAO Hua-tuo¹, WANG Fei², YANG Ming-zhi^{1Δ}

(1 Department of orthopedics, Yan'an People's Hospital, Yan'an, Shaanxi, 716000, China;

2 Spinal surgery, Affiliated Hospital of Yan'an University, Yan'an, Shaanxi, 716000, China)

ABSTRACT Objective: To study the effect of calcitonin on the amino terminal elongation peptide of type I collagen and type I collagen C-terminal peptide β degradation products was applied after thoracolumbar spine fracture. **Methods:** 80 patients with thoracolumbar spine fracture from March 2014 to May 2016 in our hospital were randomly divided into the observation group and the control group with 40 cases in each group. They were treated with minimally invasive percutaneous pedicle screw fixation, and the control group was given routine treatment after operation, and the observation group was given salmon calcitonin treatment after operation. The bone mineral density, amino terminal elongation peptide of type I collagen, type I collagen C-terminal peptide β degradation products, visual analog pain score (VAS) score, Oswestry disability index score (ODI) score, Harris score fracture healing time and incidence of adverse reactions were compared between two groups. **Results:** After treatment, the bone density and Harris score in the observation group was significantly higher than those of the control group ($P<0.05$); while the amino terminal elongation peptide of type I collagen, type I collagen C-terminal peptide β degradation products, VAS score and ODI score were lower than those of the control group ($P<0.05$); the fracture healing time in the observation group was shorter that of the control group ($P<0.05$); the incidence of adverse reactions (7.50%) showed no significant difference compared with that of the control group (10.00%) ($P>0.05$). **Conclusion:** The use of salmon calcitonin after thoracolumbar spine fracture can effectively improve the bone density of patients, promote the healing time of fracture factors With high safety.

Key words: Thoracolumbar spine fracture; Calcitonin; Type I collagen amino terminal prolonging peptide; Type I collagen C endopeptide is a degradation product

Chinese Library Classification(CLC): R683 **Document code:** A

Article ID: 1673-6273(2019)18-3550-04

* 基金项目:陕西省自然科学基金项目(2008K14-1)

作者简介:张中平(1976-),男,本科,副主任医师,研究方向:脊柱病微创治疗

Δ 通讯作者:杨明智(1986-),男,硕士研究生,研究方向:脊柱退变,电话:15991576396, E-mail: ascv689@126.com

(收稿日期:2019-01-21 接受日期:2019-02-18)

前言

胸腰椎由于外力造成骨质连续性的破坏是最为常见的脊柱损伤,患者常合并神经功能损伤,大部分致伤因素为高能损伤,常合并其他脏器损伤,给治疗带来极大的困难^[1,2]。保守治疗是目前临床上针对稳定且无神经功能损害的胸腰椎脊柱骨折患者的首选治疗方式,但对于合并神经功能损伤严重的胸腰椎脊柱骨折,早期采取手术治疗,积极解除神经压迫是促进脊柱恢复的重要手段^[3,4]。大多数使用微创经皮椎弓根螺钉内固定术治疗的效果显著,有利于患者恢复,但由于骨折部位的损伤,骨密度的降低。因此,需要一种药物来弥补此缺点^[5,6]。鲑鱼降钙素属一种人工降钙制剂,在临床上可发挥抑制骨吸收、促进成骨细胞增生等作用^[7,8]。本研究主要探讨了鲑鱼降钙素对胸腰椎脊柱骨折术后 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物的影响。

1 资料与方法

1.1 一般资料

选择 2014 年 3 月至 2016 年 5 月我院收治的胸腰椎脊柱骨折患者 80 例,将其随机分为两组,每组 40 例。观察组男 26 例,女 14 例,年龄 24~62 岁,平均年龄(40.62 ± 7.28)岁。摔伤 29 例,车祸伤 7 例,挤压伤 4 例;对照组 40 例,男 21 例,女 19 例,年龄 23~61 岁,平均年龄(41.83 ± 7.69)岁,摔伤 26 例,车祸伤 9 例,挤压伤 5 例。两组患者一般资料比较差异均无统计学意义($P > 0.05$),具有可比性。

纳入标准^[9]:(1)影响检查确诊为胸腰椎骨折,无其他合并伤;(2)神经功能正常;(3)腰椎间盘正常。排除标准^[10]:(1)患有骨质疏松者;(2)受伤时间过长者;(3)椎体骨折严重脱位者。

1.2 方法

所有患者均采用经皮微创椎弓根螺钉内固定手术,对照组术后给予常规抗感染、止痛措施;观察组肌注鲑鱼降钙素(规格 1ml:50IU,厂家:Novartis Pharma Stein AG, Switzerland, 国药准字 H20090459) 50U,隔日一次。

1.3 观察指标

采用美国 GE 公司生产的采用双能 X 线骨密度仪测定患者骨密度;采用放射免疫法测定 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物,试剂盒购于瑞士罗氏公司,严格按照说明书操作。患者疼痛评分采用视觉模拟评分法^[11]进行评定;0 分表示无痛;分值越高,疼痛感越强;ODI 评分标准^[12]:分值越低,功能障碍越少;髋关节 Harris 功能评分^[13]:评分越高,功能越好;观察记录患者骨折愈合时间及不良反应发生情况。

1.4 统计学分析

以 SPSS 18.0 软件包处理实验数据,计量资料均为正态分布,用均数 $\pm$ 标准差($\bar{x} \pm s$)表示,组间比较使用独立样本 t 检验,计数资料以率表示,组间比较采用 χ^2 检验,以 $P < 0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组治疗后骨密度的比较

治疗后,观察组骨密度显著高于对照组($P < 0.05$),见表 1。

表 1 两组治疗后骨密度的比较(g/cm^2)

Table 1 Comparison of the BMD between the two groups after treatment(g/cm^2)

Groups	n	BMD	
		Before treatment	After treatment
Observation group	40	0.618 ± 0.105	0.670 ± 0.092
Control group	40	0.621 ± 0.085	0.627 ± 0.089
t		0.140	2.125
P		0.889	0.037

2.2 两组治疗后 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物水平的比较

治疗后,观察组 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 水平显著低于对照组($P < 0.05$),见表 2。

表 2 两组治疗后 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物水平的比较($\bar{x} \pm s$)

Table 2 Comparison of the amino terminal elongation peptide of type I collagen and type I collagen C-terminal peptide β degradation products between the two groups after treatment($\bar{x} \pm s$)

Groups	n	Amino terminal elongation peptide of type I collagen (ng/ml)	Type I collagen C-terminal peptide β degradation products($\mu\text{g}/\text{mL}$)
Observation group	40	52.34 ± 4.52	223.24 ± 167.25
Control group	40	94.91 ± 5.48	478.54 ± 223.13
t		37.902	5.790
P		0.000	0.000

2.3 两组治疗后 VAS 评分和 ODI 评分的比较

($P < 0.05$),见表 3。

治疗后,观察组 VAS 评分和 ODI 评分均显著低于对照组

表 3 两组治疗后 VAS 评分和 ODI 评分比较($\bar{x} \pm s$, 分)Table 3 Comparison of the VAS score and ODI score between the two groups after treatment($\bar{x} \pm s$, scores)

Groups	n	VAS score	ODI score
Observation group	40	3.87± 0.67	36.78± 5.62
Control group	40	5.21± 0.98	45.32± 6.87
t		7.139	6.085
P		0.000	0.000

2.4 两组治疗后 Harris 评分、骨折愈合时间比较

间明显短于对照组($P < 0.05$), 见表 4。

治疗后, 观察组 Harris 评分显著高于对照组, 骨折愈合时

表 4 两组治疗后 Harris 评分和骨折愈合时间比较($\bar{x} \pm s$)Table 4 Comparison of the Harris score and fracture healing time between the two groups after treatment($\bar{x} \pm s$)

Group	n	Harris score(scores)	fracture healing time(weeks)
Observation group	40	88.82± 10.12	8.34± 0.69
Control group	40	82.61± 13.67	10.96± 1.62
t		2.309	9.411
P		0.024	0.000

2.5 两组不良反应发生情况的比较

表 5。

两组不良反应发生率比较差异无统计学意义 ($P > 0.05$), 见

表 5 两组不良反应发生比较[例(%)]

Table 5 Comparison of the incidence of adverse reactions between the two groups [n(%)]

Groups	n	Stiffness of lumbar muscles	Wound infection	Abdominal pain	Total incidence rate
Observation group	40	1(2.50)	1(2.50)	1(2.50)	3(7.50)
Control group	40	2(5.00)	1(2.50)	1(2.50)	4(10.00)
χ^2		0.364	0.000	0.000	0.157
P		0.556	1	1	0.692

3 讨论

脊柱骨折是全身骨折中较为常见的类型, 由于其解剖位置具有特殊性, 因此临床上以胸腰段脊柱骨折多发, 且大部分胸腰椎骨患者合并着不同程度的神经损伤, 若得不到及时的治疗, 严重者甚至出现瘫痪^[14]。骨代谢标志物分为骨吸收标志物和骨形成标志物, I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物是国际骨质疏松症基金会推荐使用的两组骨标志物^[15,16]。I 型胶原氨基端延长肽是骨形成标志物, 主要释放于 I 型胶原, 当机体造骨细胞合成降低时, I 型胶原氨基端延长肽水平就下降; I 型胶原 C 端肽 β 降解产物反应骨吸收, 是 I 型胶原蛋白的羧基端降解产物, 骨吸收增强时, I 型胶原降解^[17,18]。

微创经皮椎弓根螺钉内固定手术在临床上具有操作简便等特点, 对运动节段部位具有修复和保护作用^[19,20], 且可促进肌肉损伤的恢复, 降低患者手术后的引流量。但在行微创经皮椎弓根螺钉内固定术后, 大多数患者会出现腰椎骨密度的骨质疏松现象^[21,22]。鲑鱼降钙素是调节钙代谢、抑制甲状旁腺素的激素之一, 已有较多报道显示其能显著降低高周转性骨病的骨钙丢失, 在骨折愈合晚期, 降钙素能促进成骨细胞的表达, 抑制软骨

性骨瘤向骨性骨瘤转换, 促进骨形成^[23,24]。

本研究结果显示使用微创经皮椎弓根螺钉内固定术后给予鲑鱼降钙素治疗的患者骨密度明显高于使用微创经皮椎弓根螺钉内固定术的患者, 分析原因是因为鲑鱼降钙素可以抑制破骨细胞活性的同时还能抑制破骨细胞前提融合形成成熟的破骨细胞, 防止骨量的丢失^[25,26]。此外, 使用微创经皮椎弓根螺钉内固定术后给予鲑鱼降钙素治疗的患者 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物明显低于使用微创经皮椎弓根螺钉内固定术的患者, 提示鲑鱼降钙素可以有效改善患者 I 型胶原氨基端延长肽、I 型胶原 C 端肽 β 降解产物的指标, 分析原因是因为鲑鱼降钙素与下丘脑网状结构的降钙素受体特异性结合, 提高痛阈, 同时增加了脑内和外周 β 内啡肽水平^[27,28]。使用微创经皮椎弓根螺钉内固定术后给予鲑鱼降钙素治疗的患者 VAS 评分和 ODI 评分明显低于使用微创经皮椎弓根螺钉内固定术的患者, 这可能与鲑鱼降钙素针剂良好镇痛效果有关。而使用微创经皮椎弓根螺钉内固定术后给予鲑鱼降钙素治疗的患者 Harris 评分高于使用微创经皮椎弓根螺钉内固定术的患者, 骨折愈合时间明显较低。分析原因是因为鲑鱼降钙素能有效的减轻患者疼痛感, 患者的活动增加后, 进一步影响了

Harris 评分^[29,30]。此外,术后给予鲑鱼降钙素并未增加患者的不良反应,具有较高安全性。

综上所述,鲑鱼降钙素用于胸腰椎脊柱骨折术后可有效改善患者骨密度,促进骨折愈合且不会增加不良反应。

参考文献(References)

- [1] Kim K, Isu T, Morimoto D, et al. Incidental Idiopathic Bilateral Pedicle Fracture - Case Report and Literature Review [J]. NMC Case Rep J, 2018, 6(1): 35-37
- [2] Yabuno S, Yunoki M, Kanda T, et al. A Case of Nonconsecutive Multiple-level Lumbar Spondylolysis Successfully Treated with Single-level Repair of the Pars Interarticularis [J]. NMC Case Rep J, 2018, 6(1): 29-34
- [3] Ramos L, Piedra M, Muñoz P, et al. Bone mineral density evolution and incidence of fractures in a cohort of patients with primary hyperparathyroidism treated with parathyroid surgery vs active surveillance during 6 years of follow-up[J]. Endocrinol Diabetes Nutr, 2019, 66(1): 41-48
- [4] Mantovani A, Dauriz M, Gatti D, et al. Systematic review with meta-analysis: non-alcoholic fatty liver disease is associated with a history of osteoporotic fractures but not with low bone mineral density[J]. Aliment Pharmacol Ther, 2019, 49(4): 375-388
- [5] Medagam NR, Dhillion CS, Dwivedi R, et al. Rare Case of Bilateral Pure Facet Joint Dislocation of Upper Lumbar Spine without Facet Fracture: A Case Report[J]. J Orthop Case Rep, 2018, 8(3): 58-60
- [6] Koutsierimpas C, Alpantaki K, Chatzinikolaidou M, et al. The effectiveness of biodegradable instrumentation in the treatment of spinal fractures[J]. Injury, 2018, 49(12): 2111-2120.
- [7] Sladek S, Kearney C, Crean D, et al. Intra-articular delivery of a nanocomplex comprising salmon calcitonin, hyaluronic acid, and chitosan using an equine model of joint inflammation [J]. Drug Deliv Transl Res, 2018, 8(5): 1421-1435
- [8] Adeyemi WJ, Olayaki LA. Effects of Salmon Calcitonin and Omega - 3 Fatty Acids on Glucoregulatory Indices, Lipid Profile and Antioxidant Markers in Experimental Knee Osteoarthritis in Wistar Rats[J]. Niger J Physiol Sci, 2017, 32(2): 179-188
- [9] Zidan I, Khedr W, Fayed AA, et al. Retroperitoneal Extrapleural Approach for Corpectomy of the First Lumbar Vertebra : Technique and Outcome[J]. J Korean Neurosurg So, 2019, 62(1): 61-70
- [10] Anderson KB, Holloway-Kew KL, Mohebbi M, et al. Is trabecular bone score less affected by degenerative-changes at the spine than lumbar spine BMD?[J]. Arch Osteoporos, 2018, 13(1): 127
- [11] Park MS, Kang SH, Cho YJ, et al. Rapid Healing and Remodeling Process of Pediatric Seat-Belt Fracture without Surgical Treatment[J]. Korean J Neurotrauma, 2018, 14(2): 169-172
- [12] Iguacel I, Miguel-Berges ML, Gó mez-Bruton A, et al. Veganism, vegetarianism, bone mineral density, and fracture risk: a systematic review and meta-analysis[J]. Nutr Rev, 2019, 77(1): 1-18
- [13] Li CY, Chang CL, Tai TW. Incidence and risk factors for hip fracture in elderly patients undergoing lumbar spine surgery: a nationwide database study with 11-year follow-up [J]. Osteoporos Int, 2018, 29(12): 2717-2723
- [14] D'Oro A, Buser Z, Brodke DS, et al. Trends and Costs of External Electrical Bone Stimulators and Grafting Materials in Anterior Lumbar Interbody Fusion[J]. Asian Spine J, 2018, 12(6): 973-980
- [15] Brayda-Bruno M, Albano D, Cannella G, et al. Endplate lesions in the lumbar spine: a novel MRI-based classification scheme and epidemiology in low back pain patients[J]. Eur Spine J, 2018, 27(11): 2854-2861
- [16] Cherian KE, Kapoor N, Asha HS, et al. Influence of Different Reference Databases on Categorization of Bone Mineral Density: A Study on Rural Postmenopausal Women from Southern India [J]. Indian J Endocrinol Metab, 2018, 22(5): 579-583
- [17] D'Oro A, Buser Z, Brodke DS, et al. Trends and Costs of External Electrical Bone Stimulators and Grafting Materials in Anterior Lumbar Interbody Fusion[J]. Asian Spine J, 2018, 12(6): 973-980
- [18] Wang Y, Jia G, Song J, et al. Comparative Efficacy of Alendronate upon Vertebral Bone Mineral Density and Fracture Rates in East Asians Versus Non-East Asians with Postmenopausal Osteoporosis: A Systematic Review and Meta-Analysis[J]. Horm Metab Res, 2018, 50(10): 738-746
- [19] Sadrameli SS, Jafrani R, Staub BN, et al. Minimally Invasive, Stereotactic, Wireless, Percutaneous Pedicle Screw Placement in the Lumbar Spine: Accuracy Rates With 182 Consecutive Screws[J]. Int J Spine Surg, 2018, 12(6): 650-658
- [20] Fukaya K, Hasegawa M. Oblique Lumbar Interbody Fusion Combined with Minimally Invasive Percutaneous Posterior Instrumentation for Adult Spinal Deformity [J]. No Shinkei Geka, 2018, 46(9): 771-781
- [21] Shao RX, Chen BY, Zhou H, et al. Treatment of thoracolumbar burst fractures with intelligent inflated reduction combined with percutaneous pedicle screw fixation [J]. Zhongguo Gu Shang, 2018, 31(8): 698-702
- [22] Kouyoumdjian P, Gras-Combe G, Grelat M, et al. Surgeon's and patient's radiation exposure during percutaneous thoraco-lumbar pedicle screw fixation: A prospective multicenter study of 100 cases [J]. Orthop Traumatol Surg Res, 2018, 94(5): 597-602
- [23] Hibbins AR, Govender M, Indermun S, et al. In Vitro-In Vivo Evaluation of an Oral Ghost Drug Delivery Device for the Delivery of Salmon Calcitonin[J]. J Pharm Sci, 2018, 107(6): 1605-1614
- [24] Kilinc E, Dagistan Y, Kukner A, et al. Salmon calcitonin ameliorates migraine pain through modulation of CGRP release and dural mast cell degranulation in rats [J]. Clin Exp Pharmacol Physiol, 2018, 45(6): 536-546
- [25] Adeyemi WJ, Olayaki LA. Effects of single or combined administration of salmon calcitonin and omega-3 fatty acids vs. diclofenac sodium in sodium monoiodoacetate-induced knee osteoarthritis in male Wistar rats [J]. J Basic Clin Physiol Pharmacol, 2017, 28(6): 573-582
- [26] Filipović B, Šošić-Jurjević B, Ajdžanović V, et al. Response of trabecular bone, thyroid C and follicular cells to synthetic salmon calcitonin in middle-aged orchidectomized male rats[J]. J Anat, 2017, 230(6): 787-795
- [27] Peña-Rodríguez ZA, Haro-García M, Benito-Navarro JR. Nasal osteoma and inhaled salmon calcitonin: Coincidence or consequence [J]. Acta Otorrinolaringol Esp, 2017, 68(6): 366-368

- with essential arterial hypertension [J]. Zh Nevrol Psikhiatr Im S S Korsakova, 2018, 118(10): 115-121
- [10] Moll M, Christmann RB, Zhang Y, et al. Patients with systemic sclerosis-associated pulmonary arterial hypertension express a genomic signature distinct from patients with interstitial lung disease [J]. J Scleroderma Relat Disord, 2018, 3(3): 242-248
- [11] Kuang ZM, Wang Y, Feng SJ, et al. Association Between Plasma Homocysteine and Microalbuminuria in Untreated Patients with Essential Hypertension: a Case-Control Study[J]. Kidney Blood Press Res, 2017, 42(6): 1303-1311
- [12] Ma L, Li L, Tang Z. Epidemiological characteristics of hyperhomocysteinemia and H-type hypertension in the elderly in Beijing, China[J]. Clin Exp Hypertens, 2017, 39(7): 640-644
- [13] 杨旭颖,高飞,刘彦虹.高同型半胱氨酸血症和类风湿关节炎的关系[J].国际检验医学杂志, 2016, 37(5): 635-636
- [14] 张志敏,赵连友,卢凡,等.高同型半胱氨酸对高血压大鼠心肌细胞 GRP78 和 CHOP 表达及左室肥厚的影响[J].中国循证心血管医学杂志, 2014, 25(2): 223-226, 228
- [15] Xu H, Zheng H, Huang J, et al. T-cell subsets are associated with serum homocysteine concentration in patients with essential? hypertension[J]. Clin Exp Hypertens, 2017, 39(4): 377-381
- [16] Zhong F, Zhuang L, Wang Y, et al. Homocysteine levels and risk of essential hypertension: A meta-analysis of published epidemiological studies[J]. Clin Exp Hypertens, 2017, 39(2): 160-167
- [17] Tang Z, Xiao L, Wang JQ, et al. Analysis of metabolism-related indicators and MTHFR gene polymorphism in patients with H-type hypertension[J]. Minerva Med, 2017, 108(2): 103-107
- [18] Liu J, Liu H, Zhao H, et al. Relationship between cardio-ankle vascular index and homocysteine in hypertension subjects with hyperhomocysteinemia[J]. Clin Exp Hypertens, 2016, 38(7): 652-657
- [19] Chen Z, Wang F, Zheng Y, et al. H-type hypertension is an important risk factor of carotid atherosclerotic plaques [J]. Clin Exp Hypertens, 2016, 38(5): 424-428
- [20] Jiang S, Li J, Zhang Y, et al. Methylenetetrahydrofolate reductase C677T polymorphism, hypertension and risk of stroke: a prospective, nested case-control study[J]. Int J Neurosci, 2017, 127(3): 253-260
- [21] Fottrell E, Ahmed N, Shaha SK, et al. Distribution of diabetes, hypertension and non-communicable disease risk factors among adults in rural Bangladesh: a cross-sectional survey [J]. BMJ Glob Health, 2018, 3(6): e000787
- [22] Momin M, Li JP, Zhang Y, et al. Body mass index is inversely associated with arterial stiffness in Chinese adults with primary hypertension: results from the China Stroke Primary Prevention Trial (CSPPT)[J]. Clin Exp Hypertens, 2017, 9(5): 394-401
- [23] Gang L, Yanyan Z. Increased neutrophil to lymphocyte ratio in persons suffering from hypertension with hyperhomocysteinemia[J]. Hypertens Res, 2016, 39(8): 606-611
- [24] 马素霞,张红,张丽英,等.血清同型半胱氨酸与老年高血压患者左心室肥厚关系[J].中华实用诊断与治疗杂志, 2016, 30(1): 60-61
- [25] Qin X, Li J, Zhang Y, et al. Effect of folic acid supplementation on risk of new-onset diabetes in adults with hypertension in China: Findings from the China Stroke Primary Prevention Trial (CSPPT)[J]. J Diabetes, 2016, 8(2): 286-294
- [26] 莫艾. 马来酸依那普利叶酸片对于轻、中度高血压患者降压、降 HCY 的临床效果与安全性[J].中国实用医药, 2016, 11(3): 141-142
- [27] 罗羽慧,封杰,崔坤,等.马来酸依那普利叶酸片治疗短暂性脑缺血发作伴 H 型高血压的临床研究[J].中国药房, 2017, 28(2): 222-224
- [28] 宋开翠.马来酸依那普利叶酸片治疗 H 型高血压疗效观察[J].中西医结合心脑血管病杂志, 2016, 14(19): 2298-2300
- [29] 孟胜喜,霍清萍,梁芳,等.稳消 III 号方联合马来酸依那普利叶酸片治疗 H 型高血压的临床研究 [J]. 中西医结合心脑血管病杂志, 2016, 14(16): 1882-1885
- [30] 赵宝华,张硕锐,李长明,等.叶酸辅助治疗对 H 型高血压患者同型半胱氨酸水平及脑卒中发病率的影响 [J]. 中国药业, 2018, 27(5): 39-41

(上接第 3553 页)

- [28] Malmos KG, Bjerring M, Jessen CM, et al. How Glycosaminoglycans Promote Fibrillation of Salmon Calcitonin[J]. J Biol Chem, 2016, 291(32): 16849-16862
- [29] Poursina N, Vatanara A, Rouini MR, et al. The effect of excipients on the stability and aerosol performance of salmon calcitonin dry powder inhalers prepared via the spray freeze drying process [J]. Acta Pharm, 2016, 66(2): 207-218
- [30] Maison O, Pierre S, Charpiat B, et al. Seizure after salmon calcitonin administration: A case report[J]. Therapie, 2016, 71(5): 529-531