

血尿酸与骨密度相关性的研究进展

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摘要: 尿酸是嘌呤代谢的最终产物, 是人体内一种重要的内源性抗氧化剂, 在氧化应激方面发挥重要作用, 而氧化应激是骨质疏松形成的一个独立的危险因素, 因此, 血尿酸与骨量丢失可能存在某种相关性。近年来, 国内外对血尿酸与骨密度相关性的研究较多, 但其确切关系仍存在争议。本文主要从不同人群血尿酸与骨密度相关性、二者相关性的可能机制、及其存在的争议等问题进行阐述, 以期能进一步加深对二者的认识, 为临床研究提供新的思路。

关键词: 血尿酸; 骨密度; 骨质疏松

Research progress on the relationship between serum uric acid and bone mineral density

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Abstract: Uric acid is the end product of purine metabolism. It is also an important endogenous antioxidant in the body and plays an important role in oxidative stress, which is an independent risk factor for osteoporosis. Therefore, there may be some correlations between serum uric acid and bone loss. In recent years, there are many researches on the correlations between serum uric acid and bone mineral density in both China and overseas, but the exact relationship is still controversial. This paper mainly elaborates the relationship between serum uric acid and bone mineral density in different populations, the possible mechanisms, and the controversy on their correlation, etc., in order to deepen the understanding of the two and to provide new ideas for research on clinical management.

Key words: Serum uric acid; Bone mineral density; Osteoporosis

尿酸是嘌呤代谢的最终产物, 人体内血尿酸具有两重性: 首先作为还原物质参与机体的氧化还原反应, 但当其升高到一定水平时可转变为促氧化剂。研究表明原发性骨质疏松与氧化应激或循环中抗氧化剂水平下降相关, 临床上骨质疏松的诊断主要依靠骨密度, 因此, 血尿酸与骨密度可能存在某种相关性, 本文对近年研究做一综述, 以期为临床研究提供一定的依据。

1 尿酸的代谢及作用

人体中的尿酸 80% 来源于内源性嘌呤代谢, 来源于富含嘌呤或核酸蛋白食物的仅占 20%, 主要经

肾脏从尿液中排泄。正常人血浆中尿酸水平女性 100 ~ 300 $\mu\text{mol/L}$ (1. 6 ~ 5. 0 mg/dL), 男性为 150 ~ 380 $\mu\text{mol/L}$ (2. 5 ~ 6. 4 mg/dL)。血尿酸具有两重性^[1,2]: 在体内尿酸作为一种还原物质参与机体的氧化还原反应, 具有有抗氧化、抗 DNA 损伤的作用; 但当体内血尿酸水平升高到一定水平时, 尿酸可由抗氧化剂转变为促氧化剂, 导致血管平滑肌增生、内皮功能紊乱等。

2 骨质疏松

骨质疏松症是一种以骨量减少和骨微结构被破坏为特征, 导致脆性增加和易于骨折的代谢性骨病。原发性骨质疏松症发病原因有两种: 一方面是更年期卵巢功能的下降、性激素水平的缺乏; 另一方面是氧化应激或循环中抗氧化剂水平下降, 这可能

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是老年骨质疏松症发生的主要原因。与正常人相比,骨质疏松症患者血中抗氧化剂活性下降、氧化应激反应较强^[3]。

3 血尿酸与骨密度的相关性

大量研究表明,血尿酸可能与多种疾病的发病过程相关,如:心脑血管疾病、代谢综合征、肾脏疾病、慢性心力衰竭等^[4-6],但也有研究证实,血尿酸可以作为抗氧化剂参与氧化应激反应,对人体起到一定的保护作用,比如多发性硬化、肌萎缩性侧索硬化症、阿尔兹海默病等^[7-9]。近年的研究发现氧化应激增加、循环中抗氧化剂水平下降均与骨密度减低及骨质疏松症相关,尿酸作为一种抗氧化剂是否可以提高骨密度,改善骨质疏松、减少骨质疏松性骨折的发生,目前仍存在一定的争议。

3.1 2 型糖尿病患者血尿酸与骨密度的相关性

大多数 2 型糖尿病患者均存在高尿酸血症,中老年 2 型糖尿病患者,无论男性还是绝经后女性,血尿酸与多部位的骨密度呈正相关,这在临床上均有报道^[10-12],正常体检人群中也有类似发现^[13]。有学者^[14]对 621 例中国男性 2 型糖尿病患者的血尿酸与 BMD 相关性进行研究发现,在调整多种混杂因素后,高水平的血尿酸与较高的骨密度、较低风险的骨质疏松是相关的。阮园等^[15]在 200 例老年糖尿病患者的研究中发现,血尿酸与腰椎 BMD 呈正相关,是影响腰椎 BMD 的独立危险因素,其他学者^[16]在绝经女性 2 型糖尿病患者中得到类似的结论。

3.2 绝经前后女性、老年男性血尿酸与骨密度的相关性

骨质疏松症女性多发,目前主要认为与性激素水平的下降有关,围绝经期女性成为国内外学者的重点研究对象。日本学者^[17]对 615 例日本绝经前后女性进行研究,发现在调整混杂因素后血尿酸与腰椎 BMD 呈正相关,且二者呈线性相关。韩国学者^[18]对 7 502 个健康绝经女性进行血尿酸与 BMD 的研究,发现血尿酸和各部位的 BMD 均呈正相关,较高的血尿酸水平往往伴随着较高的 BMD、较低的骨转换以及较低的椎体骨折发生率,随之进行的体外试验也证明尿酸可减少破骨细胞的生成,减少破骨细胞前体活性氧的产生,且呈剂量依赖性,因此,尿酸作为一种抗氧化剂可在绝经女性骨代谢中发挥保护性作用。意大利学者在一篇系统分析中指出:血尿酸与 BMD、骨折是独立相关的,是骨代谢紊乱的一个保护性因子,血尿酸升高 1 个标准差,可减少

随访过程(3 年)中骨折的发生率,男女之间没有太大差异。国内学者^[19]认为血尿酸是 50 岁以上的男性及绝经女性骨质疏松、骨量减少的保护性因素,高水平的血尿酸与骨质疏松症及骨量减少发生率下降相关。澳大利亚学者^[20]将体重分为瘦体重和脂肪量,对 356 名绝经前后的双胞胎女性进行约 9.7 年的随访,发现较高的血尿酸水平是绝经前后女性骨量丢失的保护性因素,不受身体成分指标的影响,即与瘦体重和脂肪量无关。但是,意大利另一学者^[21]发现初次治疗的绝经后骨质疏松女性患者,血尿酸与所有的肥胖指数(BMI、脂肪量、腹围、腹部内脏脂肪面积)成正相关,血尿酸与骨代谢指标的相关性依赖于这些混杂因素,血尿酸与股骨 BMD 的相关性在一定程度上可以用混杂因素(肥胖指数)来解释。

除绝经女性外,老年男性也是骨质疏松症的高发人群。Nabipour 等^[22]对 1705 例 70 岁以上的老年男性居民进行研究,调整混杂因素后发现血尿酸和各部位的 BMD 均存在相关性,高水平的血尿酸往往伴随着较高的 BMD 及椎体、非椎体骨折发生率的下降。韩国学者 Kim 等^[23]对 16078 例 50 岁以上男性进行 3 年随访,发现基线血尿酸水平与骨质疏松性骨折是相关的,血尿酸是韩国男性脆性骨折发生的保护性因子,与大多数学者研究结果一致。另有学者^[24]发现,对于老年男性血尿酸水平升高和髌部骨折发生率增加是相关的;而另一学者发现老年男性人群中,较高的血尿酸水平与意外的非椎体骨折发生风险的下降相关,但除外髌部骨折^[25],血尿酸与老年男性髌部骨折的相关性仍待进一步研究。

3.3 骨质疏松患者血尿酸与骨密度相关性

大多数观察性临床研究认为血尿酸是骨质疏松症的保护性因素,那么在骨质疏松症患者中血尿酸与骨密度关系如何呢。Chen 等^[26]253 例原发性骨质疏松症患者中发现,血尿酸与腰椎 BMD、25-OH 维生素 D 呈正相关,且有脆性骨折史的绝经女性比无脆性骨折史的女性血尿酸水平要低。不同类型的骨质疏松患者的血尿酸与不同部位的 BMD 有不同的相关性,国内学者^[27]发现:I 型骨质疏松症 BMD 同血脂密切相关,血尿酸与股骨颈、大转子部位 BMD 相关;II 型骨质疏松症 BMD 与血脂之间无明显相关性,与血尿酸有一定的相关性,血尿酸与 L₂₋₄ 部位 BMD 相关。国内学者陈琳等^[28]认为在校正年龄、性别、体重指数后,原发性骨质疏松症患者血清尿酸水平与腰椎骨密度相关,但与髌部及股骨颈 BMD 无关,尿酸不是骨折的独立危险因素。Veronese 等^[29]对 1586 名老

年人随访 4.4 ± 1.2 年,发现基线血尿酸水平与新发骨质疏松性骨折的发生无关。

4 血尿酸与骨密度相关性的争议

有学者认为目前已发表的关于血尿酸与 BMD 相关性的研究,大多数为观察性研究,由于一些不可测量的混杂因素的存在,这些学者没有对血尿酸与 BMD 进行深入的研究,因此,对其相关性提出质疑。国内学者利用孟德尔随机化研究对上海地区 1322 例汉人(绝经后女性、老年男性)临床资料进行统计学分析^[30],在普通的观察性分析中发现血尿酸与骨代谢相关性指标(BMD、骨质疏松性骨折)有很强的相关性,但是孟德尔随机化分析提示血尿酸与 BMD 及其他骨相关的表型没有因果关系;美国学者 Dalbeth 等^[31]对来自弗雷明汉心脏研究中心的 2501 名患者进行孟德尔随机化分析后得出了相同的结论。另有学者^[32]发现在美国 30 岁以上的普通人中,不论是男性,还是绝经前后的女性,在未调整混杂因素时,血尿酸与各部位(股骨颈、全髋、腰椎)BMD 均呈正相关,调整各种混杂因素(如:年龄、BMI、黑色人种、酒精摄入、肾小球滤过率、血清碱性磷酸酶、C 反应蛋白等)后,二者便无相关性,随后进行的试验性高尿酸血症小鼠试验,也证实二者没有相关性。

5 血尿酸与骨质疏松发生机制的研究

血尿酸引起骨密度增加的具体机制仍不清楚,目前大多数学者认为可能与以下因素有关:①体内氧化应激增加或抗氧化应激能力下降,抑制了成骨细胞活性^[33],进而减少骨形成,促进骨量丢失,降低 BMD,尿酸作为抗氧化剂可减少骨量丢失,从而增加 BMD。②有研究证明血清尿酸水平与 25(OH)D 水平成正相关^[28],因此推测血尿酸可能通过升高活性维生素 D 水平,促进钙吸收,提高骨密度。③体外实验发现,尿酸可通过下调 11B-HSD1mRNA 的表达,上调 BMP-2 mRNA、cbfa1/Run × 2 的表达,促进 hBMSCs 向成骨细胞增殖和分化,减少破骨细胞前体产生氧自由基^[34-36]。

血尿酸水平升高会导致高尿酸血症,严重时导致痛风,研究证明血尿酸过高会导致骨密度下降,引起骨质疏松^[37],而痛风又是骨折的危险因子^[38]。骨质疏松症发病机制复杂,影响因素较多,大多数潜在的混杂因素无法测量,血尿酸与骨密度是否存在相关性,较高的血尿酸水平是否可提高骨密度,血尿酸

控制在什么水平才能使患者受益最大,目前仍需进一步的临床及基础研究来证实。

【 参 考 文 献 】

[1] Jin M, Yang F, Yang I, et al. Uric acid, hyperuricemia and vascular diseases. *Frontiers in Bioscience*, 2011, 17(1):656-669.

[2] 王颜刚,阎胜利,李长贵,等. 山东沿海居民血尿酸水平与心血管疾病危险因素的关系. *中华内分泌代谢杂志*, 2009, 25(2):159-163.

Wang YG, Yang SL, Li CG, et al. Correlation between serum uric acid and cardiovascular risk factors in Shandong coastal inhabitants. *Chinese Journal of Endocrinology and Metabolism*, 2009, 25(2):159-163. (in Chinese)

[3] Sendur OF, Turan Y, Tastaban E, et al. Antioxidant status in patients with osteoporosis: a controlled study. *Joint Bone Spine Revue Du Rhumatisme*, 2009, 76(5):514-518.

[4] Kawai T, Ohishi M, Takeya Y, et al. Serum uric acid is an independent risk factor for cardiovascular disease and mortality in hypertensive patients. *Hypertension Research*, 2012, 35(11):1087-1092.

[5] Zhang Q, Zhang C, Song X, et al. A longitudinal cohort based association study between uric acid level and metabolic syndrome in Chinese Han urban male population. *BMC Public Health*, 2012, 12(1):1-8.

[6] Chiou WK, Huang DH, Wang MH, et al. Significance and association of serum uric acid (UA) levels with components of metabolic syndrome (MS) in the elderly. *Archives of Gerontology & Geriatrics*, 2012, 55(3):724-728.

[7] Massa J, O'Reilly E, Munger KL, et al. Serum uric acid and risk of multiple sclerosis. *Journal of Neurology*, 2009, 256(10):1643-1648.

[8] Keizman D, Ishshalom M, Berliner S, et al. Low uric acid levels in serum of patients with ALS: further evidence for oxidative stress. *Journal of the Neurological Sciences*, 2009, 285(1-2):95-99.

[9] Andreadou E, Nikolaou C, Gournaras F, et al. Serum uric acid levels in patients with Parkinson's disease: Their relationship to treatment and disease duration. *Clinical Neurology & Neurosurgery*, 2009, 111(9):724-728.

[10] 刘咏萍,赵娜,李玉妹,等. 中老年 2 型糖尿病患者骨密度与尿酸、胰岛素抵抗关系的研究. *中国骨质疏松杂志*, 2016, 22(3):343-347.

Liu YP, Zhao N, Li YS, et al. Bone mineral density is associated with uric acid and insulin resistance in elderly patients with type 2 diabetes. *Chin J Osteoporos*, 2016, 22(3):343-347. (in Chinese)

[11] 崔晶,杨乃龙,朱晓琳,等. 老年 2 型糖尿病患者血尿酸与骨密度关系的研究. *中国骨质疏松杂志*, 2011, 17(12):1052-1055.

Cui J, Yang NL, Zhu XL, et al. Association between uric acid

- and bone mineral density in elderly people with type 2 diabetes mellitus. *Chin J Osteoporos*, 2011, 17 (12) : 1052-1055. (in Chinese)
- [12] 赵娜,李素梅,方星星,等.老年糖尿病患者骨密度与血尿酸水平的相关研究.中国骨质疏松杂志,2014,20(7):784-788. Zhao N, Li SM, Fang XX, et al. Study of the relationship between bone mineral density and serum uric acid in senile diabetic patients. *Chin J Osteoporos*, 2014, 20(7):784-788. (in Chinese)
- [13] 陈伟军,肖婧,邹佳楠,等.中年体检人群血尿酸与骨密度及骨代谢标记物的相关性.第二军医大学学报,2015,36(10):1056-1062. Chen WJ, Xiao J, Zou JN, et al. Correlation of serum uric acid with bone mineral density and bone metabolic markers in middle-age Chinese physical examination population. *Academic Journal of Second Military Medical University*, 2015, 36 (10) : 1056-1062. (in Chinese)
- [14] Zhao DD, Jiao PL, Yu JJ, et al. Higher serum uric acid is associated with higher bone mineral density in chinese men with type 2 diabetes mellitus. *International Journal of Endocrinology*, 2016, 2016(6):2528956.
- [15] 阮园,吴天凤,袁放,等.老年 2 型糖尿病血尿酸水平与骨密度的相关性研究.中国临床药理学与治疗学,2015,20(5):567-570. Yuan Y, Wu TF, Yuan F, et al. Relationship between uric acid and bone mineral density in elderly type 2 diabetes. *Chinese Journal of Clinical Pharmacology and Therapeutics*, 2015, 20(5):567-570. (in Chinese)
- [16] 郝雅斌,洪旭.绝经后女性 2 型糖尿病患者血尿酸与骨密度相关性研究.中国骨质疏松杂志,2014,20(12):1421-1424. Hao YB, Hong X. Association between uric acid and bone mineral density in postmenopausal women with type 2 diabetes. *Chin J Osteoporos*, 2014, 20(12):1421-1424. (in Chinese)
- [17] Ishii S, Miyao M, Mizuno Y, et al. Association between serum uric acid and lumbar spine bone mineral density in peri- and postmenopausal Japanese women. *Osteoporosis International*, 2014, 25(3):1099-1105.
- [18] Ahn SH, Lee SH, Kim BJ, et al. Higher serum uric acid is associated with higher bone mass, lower bone turnover, and lower prevalence of vertebral fracture in healthy postmenopausal women. *Osteoporosis International*, 2013, 24(12):2961-2970.
- [19] Lin X, Zhao C, Qin A, et al. Association between serum uric acid and bone health in general population: a large and multicentre study. *Oncotarget*, 2015, 6(34):35395-35403.
- [20] Makovey J, Macara M, Jian SC, et al. Serum uric acid plays a protective role for bone loss in peri- and postmenopausal women: a longitudinal study. *Bone*, 2013, 52(1):400-406.
- [21] Pirro M, Mannarino MR, Bianconi V, et al. Uric acid and bone mineral density in postmenopausal osteoporotic women: the link lies within the fat. *Osteoporosis International*, 2016;1-9.
- [22] Nabipour I, Sambrook PN, Blyth FM, et al. Serum uric acid is associated with bone health in older men: a cross-sectional population-based study. *Journal of Bone and Mineral Research*, 2011, 26(5):955-964.
- [23] Kim BJ, Baek S, Ahn SH, et al. Higher serum uric acid as a protective factor against incident osteoporotic fractures in Korean men: a longitudinal study using the National Claim Registry. *Osteoporosis International*, 2014, 25(7):1837-1844.
- [24] Mehta T, Sarnak MJ, et al. Serum urate levels and the risk of hip fractures: data from the Cardiovascular Health Study. *Metabolism Clinical & Experimental*, 2015, 64(3):438-446.
- [25] Lane NE, Parimi N, Lui LY, et al. Association of serum uric acid and incident nonspine fractures in elderly men: the osteoporotic fractures in men (MrOS) study. *Journal of Bone and Mineral Research*, 2014, 29(7):1701-1707.
- [26] Chen L, Peng Y, Fang F, et al. Correlation of serum uric acid with bone mineral density and fragility fracture in patients with primary osteoporosis: a single-center retrospective study of 253 cases. *International Journal of Clinical & Experimental Medicine*, 2015, 8(4):6291-6294.
- [27] 王海风,侯再强,艾智华,等.原发性骨质疏松患者骨密度与血脂血尿酸关系的研究.第三军医大学学报,2002,24(9):1113-1114. Wang HF, Hou ZQ, Ai ZH, et al. Correlation between bone mineral density blood lipid and blood uric acid. *Journal of Third Military Medical University*, 2002, 24 (9) : 1113-1114. (in Chinese)
- [28] 陈琳,游利,陈瑾瑜,等.原发性骨质疏松症血清尿酸水平与骨密度、骨转换标记物及骨折的相关性研究.第十届中国南方骨质疏松论坛暨重庆市医学会骨质疏松年会论文集. 2014:1336-1345. Chen L, You L, Chen JY, et al. The relationship between serum uric acid levels and bone mineral density, bone metabolic markers and fracture in patients with primary osteoporosis. *Proceedings of the Tenth South China Osteoporosis Forum and Annual Osteoporosis Society of Chongqing Medical Association*. 2014: 1336-1345. (in Chinese)
- [29] Veronese N, Bolzetta F, De RM, et al. Serum uric acid and incident osteoporotic fractures in old people: the PRO. V. A study. *Bone*, 2015, 79:183-189.
- [30] Xiong A, Yao Q, He J, et al. No causal effect of serum urate on bone-related outcomes among a population of postmenopausal women and elderly men of Chinese Han ethnicity-a Mendelian randomization study. *Osteoporosis International*, 2016, 27(3):1031-1039.
- [31] Dalbeth N, Topless R, Flynn T, et al. Mendelian randomization analysis to examine for a causal effect of urate on bone mineral density. *Journal of Bone and Mineral Research*, 2015, 30(6):985-991.
- [32] Zhang D, Bobulescu IA, Maalouf NM, et al. Relationship between serum uric Acid and bone mineral density in the general population and in rats with experimental hyperuricemia. *Journal of Bone and Mineral Research*, 2015, 30(6):992-999.

osteoporosis based on the theory of “preventive treatment and prevention before disease onset”. Western Journal of Traditional Chinese Medicine, 2017, 30(1):69-72. (in Chinese)

[47] 罗善锋, 杨卿, 沈旭等. “治未病”理论在防治社区原发性骨质疏松症中的应用研究. 中国现代药物应用, 2015, 9(6): 247-248.

Luo SF, Yang Q, Shen X, et al. Application research on prevention and treatment of primary osteoporosis in community based on Chinese traditional prophylactic theory. Chin J Mod Drug Appl, 2015, 9(6):247-248. (in Chinese)

[48] 邢燕, 毕宏焱, 张倩楠, 等. 骨质疏松常用中成药介绍. 中国骨质疏松杂志, 2013, 19(1):83-85.

Xing Y, Bi HY, Zhang QN, et al. Introduction of common Chinese patent medicines for the treatment of osteoporosis. Chin J Osteoporosis, 2013, 19(1):83-85. (in Chinese)

[49] 罗展鹏, 王亮, 徐小文, 等. 基于数字化平台的骨质疏松健康教育及运动指导的效果评价. 实用临床医药杂志, 2016, 20(13):73-76.

Luo ZP, Wang L, Xu XW, et al. Effect assessment of osteoporosis health education and movement instruction based on the digital platform. Journal of Clinical Medicine in Practice, 2016, 20(13):73-76. (in Chinese)

[50] 聂然, 沈丽萍, 陈婷婷. 医护一体化健康教育模式在骨质疏松门诊中的应用效果. 实用临床护理学电子杂志, 2017, 2(2):47.

Nie R, Shen LP, Chen TT. Application effects of integrated health education model of medical care in osteoporosis clinic. Journal of Clinic Nursing's Practicality, 2017, 2(2):47. (in Chinese)

[51] 陈立英, 王亮, 张妍, 等. 骨质疏松门诊健康教育模式的探讨. 中国骨质疏松杂志, 2016, 22(12):1548-1550.

Chen LY, Wang L, Zhang Y, et al. To explore the model of health education at outpatient clinic in patients with osteoporosis. Chin J Osteoporosis, 2016, 22(12):1548-1550. (in Chinese)

[52] 陈莉, 王刚. 整合式健康教育在社区中老年患者骨质疏松症管理中的应用. 实用临床医药杂志, 2016, 20(22):47-50.

Chen L, Wang G. The application of integrated health education in the elderly with osteoporosis in community. Journal of Clinical Medicine in Practice, 2016, 20(22):47-50. (in Chinese)

[53] 张智海, 高冰, 刘忠厚. 应用骨折风险因子评估工具 (FRAX) 诊治骨质疏松症. 中国骨质疏松杂志, 2012, 18(7):589-595.

Zhang ZH, Gao B, Liu ZH, Fracture risk assessment tool (FRAX) for osteoporosis diagnosis and treatment. Chin J Osteoporosis, 2012, 18(7):589-595. (in Chinese)

[54] Koh LK, Sedrine WB. A simple tool to identify Asian women at increased risk of osteoporosis. Osteoporos Int, 2001, 12: 699-705.

[55] Kanis JA, Melton LJ, Christiansen C, et al. Perspective - the diagnosis of osteoporosis. Journal of Bone And Mineral Research, 1994, 9(8):1137-1141.

[56] 廖静, 马林, 周晓梅, 等. 健康管理干预骨质疏松高危人群的研究. 中国医药指南, 2011, 9(36):45-46.

Liao J, Ma L, Zhou XM, et al. Health management interventions at high risk of osteoporosis. Guide of China Medicine, 2011, 9(36):45-46. (in Chinese)

[57] 侯武姿, 杜雪平, 于溯, 等. 社区居民骨质疏松症危险因素认知状况及干预效果研究. 中国全科医学, 2015, 18(10): 1212-1215.

Hou WZ, Du XP, Yu S, et al. Community residents' awareness status of risk factors for osteoporosis and intervention effect. Chin J Gen Pract, 2015, 18(10):1212-1215. (in Chinese)

(收稿日期: 2017-06-19, 2017-07-25)

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[33] Dalbeth N, Smith T, Nicolson B, et al. Enhanced osteoclastogenesis in patients with tophaceous gout: urate crystals promote osteoclast development through interactions with stromal cells. Arthritis & Rheumatology, 2008, 58(6):1854-1865.

[34] 李百举, 杨乃龙, 宋青青, 等. 尿酸下调人骨髓间充质干细胞体外诱导为成骨细胞过程中 11 β -HSD1 的表达. 中华骨质疏松和骨矿盐疾病杂志, 2013, 6(1):50-59

Li BJ, Yang NL, Song QQ, et al. Uric acid down-regulates expression of 11 β -HSD1 in the course of hBMSCs induction into osteoblasts in vitro. Chinese Journal of Osteoporosis and Bone Mineral Research, 2013, 6(1):50-59. (in Chinese)

[35] 张山山, 杨乃龙, 徐丽丽, 等. 尿酸对人骨髓间充质干细胞成骨分化中 Cbfa1/Runx2 表达的影响. 中国骨质疏松杂志, 2013, 19(4):363-366, 344.

Zhang SS, Yang NL, Xu LL, et al. Effect of uric acid on the expression of Cbfa1/Runx2 during the osteogenic differentiation of human bone marrow mesenchymal stem cells. Chin J Osteoporos, 2013, 19(4):363-366, 344. (in Chinese)

[36] 谢婷婷, 杨乃龙, 徐丽丽, 等. 尿酸影响人骨髓间充质干细胞成骨分化过程中 BMP-2 表达. 现代生物医学进展, 2015, 15(12):2251-2256.

Xie TT, Yang NL, Xu LL, et al. Effect of UA on the Expression of BMP-2 during the Osteogenic Differentiation Of Human Bone Marrow Mesenchymal Stem Cells. Progress in Modern Biomedicine, 2015, 15(12):2251-2256. (in Chinese)

[37] 黎荣山, 黎文军, 王勇, 等. 柳州市人群血尿酸水平与骨密度之间的关系. 中国医学创新, 2016, 13(15):138-140, 141.

Li SS, Li WJ, Wang Y, et al. The Relationship Between Blood Uric Acid Levels And Bone Mineral Density In People of Liuzhou City. Medical Innovation of China, 2016, 13(15):138-140, 141. (in Chinese)

[38] Tzeng HE, Lin CC, Wang IK, et al. Gout increases risk of fracture: A nationwide population-based cohort study. Medicine, 2016, 95(34):e4669.

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