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血清 25- 羟维生素 D 水平与儿童骨密度的相关性研究 *

赵 锋[1] 王瑞芳[1] 王 坤[2] 孙 芳[1] 魏冬冬[3] 程大伟[3] 周 瑞[4]

（1 安徽理工大学附属亳州医院 / 亳州市人民医院儿童保健门诊 安徽 亳州 236800；
2 安徽理工大学附属亳州医院 / 亳州市人民医院检验科 安徽 亳州 236800；
3 安徽理工大学附属亳州医院 / 亳州市人民医院医务部 安徽 亳州 236800；
4 蚌埠医学院第一附属医院儿科 安徽 蚌埠 233004）

摘要 目的：研究血清 25- 羟维生素 D[25-(OH)D]水平与儿童骨密度（BMD）的相关性。**方法：**选择 2017 年 1 月到 2017 年 12 月在亳州市人民医院接受健康体检的儿童 100 例作为研究对象。根据血清 25-(OH)D 水平对维生素 D（Vit D）营养状况进行分组，其中严重缺乏组 9 例，缺乏组 28 例，不足组 42 例和充足组 21 例。对比不同年龄段和不同性别儿童血清 25-(OH)D、BMD 水平以及不同 Vit D 营养状况儿童对应的 BMD 水平，并采用 Spearman 相关性分析法分析血清 25-(OH)D 水平与儿童 BMD、年龄的相关性。**结果：**5-9 岁和 10-14 岁儿童的血清 25-(OH)D 及 BMD 水平均分别低于 1-4 岁儿童，而 10-14 岁儿童又低于 5-9 岁儿童（*P<0.05*）。男童的血清 25-(OH)D 及 BMD 水平均分别高于女童，差异有统计学意义（*P<0.05*）。不足组、缺乏组、严重缺乏组儿童的 BMD 水平均分别低于充足组，且缺乏组和严重缺乏组低于不足组，严重缺乏组又低于缺乏组（*P<0.05*）。根据 Spearman 相关性分析结果显示，血清 25-(OH)D 水平与儿童 BMD 呈正相关，而与年龄呈负相关（*P<0.05*），年龄与儿童 BMD 呈负相关（*P<0.05*）。**结论：**血清 25-(OH)D 水平与儿童 BMD 呈正相关，但与年龄则呈负相关，及时补充适量的 VitD 以满足儿童的机体所需，有利于儿童健康成长。

关键词：血清；25- 羟维生素 D；儿童；骨密度；相关性

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Correlation Study between Serum 25-hydroxyvitamin D Level and Bone Mineral Density in Children*

ZHAO Feng[1], WANG Rui-fang[1], WANG Kun[2], SUN Fang[1], WEI Dong-dong[3], CHENG Da-wei[3], ZHOU Rui[4]

(1 Department of Child Health Care Clinic, The Affiliated Bozhou Hospital of Anhui University of Science and Technology /Bozhou People's Hospital, Bozhou, Anhui, 236800, China; 2 Department of Clinical Laboratory, The Affiliated Bozhou Hospital of Anhui University of Science and Technology/Bozhou People's Hospital, Bozhou, Anhui, 236800, China; 3 Department of Medical Affairs, The Affiliated Bozhou Hospital of Anhui University of Science and Technology/Bozhou People's Hospital, Bozhou, Anhui, 236800, China; 4 Department of Pediatrics, The First Affiliated Hospital of Bengbu Medical College, Bengbu, Anhui, 233004, China)

ABSTRACT Objective: To study the correlation between serum 25-hydroxyvitamin D [25- (OH)D] level and bone mineral density (BMD) in children. **Methods:** 100 children who were received physical examination in Bozhou People's Hospital from January 2017 to December 2017 were selected as the research subjects.According to the serum 25- (OH) D level, the nutritional status of vitamin D (Vit D) in children was divide into groups, including severe deficiency group with 9 cases, deficiency group with 28 cases, insufficiency group with 42 cases and sufficient group with 21 cases. The levels of serum 25-(OH)D and BMD in children with different ages and sexes were compared, and the level of BMD in children with different Vit D nutritional status was compared, the correlation between serum 25-(OH) D level and BMD, age of children was analyzed by Spearman correlation analysis. **Results:** The levels of serum 25- (OH)D and BMD in children aged 5-9 and 10-14 years old were significantly lower than those of children aged 1-4 years old, children aged 10-14 years old was significantly lower than children aged 5-9 years old (*P<0.05*). The levels of serum 25- (OH)D and BMD in boys were higher than those of girls, and the difference was statistically significant (*P<0.05*). The level of BMD of children in insufficiency group, deficiency group and severe deficiency were lower than that in sufficient group, respectively, the deficiency group and severe deficiency group was significantly lower than that of insufficiency group, the severe deficiency group was lower than that of the deficiency group (*P<0.05*). The results of Spearman correlation analysis show that serum 25-(OH)D level was positively correlated with BMD in children, but which was negatively correlated with age (*P<0.05*), age was negatively correlated with BMD in children (*P<0.05*). **Conclusion:** The level of serum 25- (OH) D is positively correlated with BMD in children, but it is negatively correlated with age. It is necessary to replenish the right amount of VitD in time to meet the needs of children's body, which is beneficial to the healthy growth of children.

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作者简介：赵锋（1983-），男，本科，主治医师，从事儿童保健方面的研究，E-mail: lxsnkl@163.com

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前言

人体的正常生活均需骨骼的支持,而维生素 D(vitamin D,Vit D)对于骨骼健康的维持具有重要的作用[1]。有报道指出,Vit D 可能与糖尿病、癌症以及自身免疫类疾病等多类慢性疾病联系紧密[2-4]。由于人体内的 Vit D 通常源自皮肤及食物,并由肝脏和肾外组织进行代谢之后产生 25- 羟维生素 D[25-hydroxyvitamin D,25-(OH)D],而 25-(OH)D 是机体中 Vit D 的主要存在形式,对其实施监测有助于反映机体中 Vit D 营养情况[5,6]。近年来发现,血清 25-(OH)D 与老年人的骨质疏松等情况有关,但关于其与儿童骨密度之间的关系的报道较少[7,8]。由于儿童处于生长发育的重要时期,若体内血清 25-(OH)D 水平较低,则可能导致 Vit D 营养状况不良,严重缺乏时甚至引起佝偻病等一系列疾病,因此分析 25-(OH)D 与儿童骨密度之间的相关性,有助于更加全面地掌握儿童的生长发育情况,帮助其科学地预防骨骼发育异常性疾病,现报道如下。

1 资料和方法

1.1 一般资料

选择 2017 年 1 月到 2017 年 12 月在亳州市人民医院接受健康体检的儿童 100 例作为研究对象。入选标准:(1) 儿童年龄≤ 14 岁;(2)体检资料数据齐全者;(3)家长均已同意此次研究,并且签署了知情同意书。排除标准:(1)存在甲状腺疾病或糖尿病,亦或是脑垂体病变及其他内分泌异常性疾病者;(2)存在成骨不全或骨肿瘤以及骨软化症等骨骼类疾病者;(3) 存在心、肝、肾等脏器的功能性障碍者;(4)有血液疾病者;(5)有皮肤性疾病而无法耐受阳光照射者。其中男 67 例,女 33 例;年龄 1-14 岁,平均(6.89± 1.23)岁,其中 1-4 岁 22 例,5-9 岁 42 例,10-14 岁 36 例。根据血清 25-(OH)D 水平进行 Vit D 营养状况分组,25- (OH)D 水平 <10 ng/mL 记为严重缺乏组 9 例,10 ng/mL≤ 25- (OH)D 水平 <20 ng/mL 记为缺乏组 28 例,20 ng/mL≤ 25-(OH)D 水平 <30 ng/mL 记为不足组 42 例,25-(OH)D 水平≥ 30 ng/mL 记为充足组 21 例。本次研究已经获得了亳州市人民医院伦理委员会的评审通过。

1.2 研究方法

统计并记录所有儿童的年龄和性别等基础资料,检测儿童的 25-(OH)D 水平及骨密度(Bone mineral density,BMD)水平,其中血清 25-(OH)D 水平的检测如下:在接受健康体检时采集儿童的空腹静脉血 3 mL, 给予 10 min 3000 r/min 的离心后将血清提取至管内,通过深圳迈瑞发光分析仪及其试剂盒采用电化学发光法检测血清 25-(OH)D 水平。BMD 的检测步骤:由医院专职医师在 18℃ -20℃ 的室温下通过 Sunlight 公司生产的 Omnisense7000P 型骨超声强度仪实施检测。检测时需对桡骨远端位置的 1/3 处亦或是胫骨中端的 1/3 处实施定位, 然后扫描该区域检测的超声传播速度,将所得数值与仪器自配的健康儿童检测值数据库进行比对,获得与年龄及性别互相匹配的有关结果,所得结果采用百分比形式表示,用于反映儿童在同类健康人群当中的骨矿化情况。

1.3 统计学方法

使用 SPSS21.0 统计软件实施数据的处理和分析, 若为计量资料,则数据用($\bar{x}\pm s$)表示,两组比较采用 t 检验,多组比较采用单因素方差分析。血清 25-(OH)D 与儿童 BMD、年龄的相关性采用 Spearman 相关性分析法,*P<0.05* 为差异有统计学意义。

2 结果

2.1 不同年龄段儿童 25-(OH)D 及 BMD 水平的对比

各年龄段儿童血清 25-(OH)D 及 BMD 水平整体比较差异有统计学意义(*P<0.05*)。5-9 岁和 10-14 岁儿童的 25-(OH)D 及 BMD 水平均分别低于 1-4 岁儿童,而 10-14 岁儿童又低于 5-9 岁儿童(*P<0.05*),见表 1。

表 1 不同年龄段儿童 25-(OH)D 及 BMD 水平的对比($\bar{x}\pm s$)

Table 1 Comparison of the levels of 25-(OH)D and BMD in children with different ages($\bar{x}\pm s$)

Age area(years old)	n	25-(OH)D(ng/mL)	BMD(%)
1-4	22	37.24± 3.67	58.63± 2.61
5-9	42	25.18± 4.66*	52.58± 3.62*
10-14	36	19.67± 3.28*△	48.47± 6.21*△
F	-	6.941	4.217
P	-	0.000	0.001

Note: compared with 1-4 years old,**P<0.05*; compared with 5-9 years old,△*P<0.05*.

2.2 不同性别儿童 25-(OH)D 及 BMD 水平的对比

男童的血清 25- (OH)D 及 BMD 水平均分别高于女童,差异有统计学意义(*P<0.05*),见表 2。

2.3 不同 Vit D 营养状况儿童对应的 BMD 水平对比

不同 Vit D 营养状况儿童的 BMD 水平整体比较差异有统计学意义(*P<0.05*)。不足组、缺乏组、严重缺乏组儿童的 BMD 水平均分别低于充足组, 且缺乏组和严重缺乏组低于不足组,严重缺乏组又低于缺乏组(*P<0.05*),见表 3。

2.4 血清 25-(OH)D 与儿童 BMD、年龄的相关性分析

Spearman 相关性分析结果显示,血清 25-(OH)D 水平与儿

童 BMD 呈正相关，而与年龄呈负相关（*P<0.05*），年龄与儿童 BMD 呈负相关（*P<0.05*），见表 4。

表 2 不同性别儿童 25-(OH)D 及 BMD 水平的对比（$\bar{x}\pm s$）

Table 2 Comparison of the levels of 25-(OH)D and BMD in children with different sexes($\bar{x}\pm s$)

Sexes	n	25-(OH)D（ng/mL）	BMD（%）
Boys	67	23.66± 7.39	53.09± 3.98
Girls	33	20.78± 4.64	49.87± 2.94
t	-	2.046	4.122
P	-	0.043	0.000

表 3 不同 Vit D 营养状况儿童对应的 BMD 水平对比（$\bar{x}\pm s$）

Table 3 Comparison of BMD levels in children with different Vit D nutritional status ($\bar{x}\pm s$)

Groups	n	BMD（%）
Sufficient group	21	62.68± 5.94
Insufficient group	42	52.66± 3.27*
Deficiency group	28	48.83± 4.06*△
Severe deficiency group	9	45.41± 4.90*△#
F	-	12.681
P	-	0.000

Note: compared with sufficient group,**P<0.05*; compared with insufficient group,△*P<0.05*; compared with deficiency group, #*P<0.05*.

表 4 血清 25-(OH)D 与儿童 BMD、年龄的相关性分析（r，*P*）

Table 4 Correlation analysis between serum 25-(OH)D and BMD, age of children(r, *P*)

Objects	BMD	Age
25-(OH)D	（0.591，0.000）	（-0.614，0.000）
BMD	-	（-0.564，0.001）

3 讨论

对于儿童的生长发育而言，Vit D 属于机体内十分重要的一类骨代谢调节性激素，其不仅能够对钙磷的代谢进行调节，而且有助于钙吸收和钙在骨骼中的沉积[9,10]。若儿童机体缺乏 Vit D，则可能导致 Vit D 缺乏型佝偻病或其他自身免疫型疾病，严重时甚至影响儿童的生长发育[11-13]。有报道指出，儿童在生长期若机体长期缺乏 Vit D，可能会引起骨骼畸形，同时也会造成骨量下降，进而导致其在老年后发生骨质疏松症的几率增大[14-16]。因此，监测 Vit D 在儿童机体中的变化情况显得十分必要。目前认为，25-(OH)D 是一种能够灵敏地反映出儿童机体中 Vit D 营养状况的指标，也是被用于临床判断 Vit D 是否缺乏的诊断指标之一[17,18]。

本研究结果发现，5-9 岁和 10-14 岁儿童的 25- (OH)D 及 BMD 水平均分别低于 1-4 岁儿童，而 10-14 岁儿童又低于 5-9 岁儿童（*P<0.05*），提示儿童的 25-(OH)D 及 BMD 水平与其年龄有关，且年龄越大的儿童 25-(OH)D 及 BMD 水平越低。分析原因，主要可能是因为伴随着儿童的年龄增长，其受到幼托机构或学校等环境的限制，在日照较多时段进行的户外活动较少，加之儿童在婴幼儿时期之后没有充足摄入奶制品和 Vit D 的补充剂，因此 25-(OH)D 及 BMD 水平逐渐降低[19-21]。此外，男童的 25-(OH)D 及 BMD 水平均分别高于女童（*P<0.05*），提示儿童的 25-(OH)D 及 BMD 水平还和性别有一定联系，且二者在男童机体中的水平相对更高。究其原因，主要是因为男童日常生活中比女童要更活跃或好动，尤其是进入到学龄期后的男童通常更为活泼，而女童则比较文静少动，致使女童机体相对缺乏 Vit D，因此 25-(OH)D 及 BMD 水平在男童机体中往往更高[22-24]。本研究结果还显示，不足组、缺乏组、严重缺乏组儿童的 BMD 水平均分别低于充足组，且缺乏组和严重缺乏组低于不足组，严重缺乏组又低于缺乏组（*P<0.05*），提示随着 Vit D 的缺乏情况加剧，儿童机体的 BMD 水平也逐渐下降。原因主要在于当 Vit D 在儿童机体中未处于正常范围时，间接地影响了 25-(OH)D 水平，由于代偿机制的作用，不断促使前破骨细胞朝着成熟性破骨细胞加速分化，致使骨量减少，最终降低了 BMD[25-27]。Yu X 等人[28]报道指出，儿童机体内 BMD 的下降也可能和 VitD 受体的基因多态性等因素有关，这也为深入开展后续研究提供了一个方向。最后，根据 Spearman 法分析显示，血清 25-(OH)D 水平与儿童 BMD 呈正相关，而与年龄呈负相关（*P<0.05*），年龄与儿童 BMD 呈负相关（*P<0.05*），再次证实了儿童机体中血清 25-(OH)D 水平与其 BMD、年龄有关，而年龄又会影响 BMD。这在王丽敏等人[29,30]的报道中也可加以佐证，儿童 BMD 与其年龄等因素密切相关。因此，临床应重视对学龄期或学龄前期儿童科学补充 Vit D。

综上所述，血清 25-(OH)D 与儿童 BMD 存在正相关，且与

儿童年龄也具有一定联系,临床应对学龄期或学龄前期儿童及时补充 Vit D,更好地促进其机体健康生长发育。

参 考 文 献(References)

[1] Borg SA, Buckley H, Owen R, et al. Early life vitamin D depletion alters the postnatal response to skeletal loading in growing and mature bone[J]. PLoS One, 2018, 13(1): e0190675

[2] Kirac D, Dincer Yazan C, Gezmis H, et al. VDBP, VDR Mutations and Other Factors Related With Vitamin D Metabolism May Be Associated With Type 1 Diabetes Mellitus [J]. Cell Mol Biol (Noisy-le-grand), 2018, 64(3): 11-16

[3] Zhu Y, Wang PP, Zhai G, et al. Association of rs2282679 A>C polymorphism in vitamin D binding protein gene with colorectal cancer risk and survival: effect modification by dietary vitamin D intake[J]. BMC Cancer, 2018, 8(1): 155

[4] Ao T, Kikuta J, Ishii M. Update on recent progress in vitamin D research. The effects of vitamin D in autoinflammatory diseases[J]. Clin Calcium, 2017, 27(11): 1551-1559

[5] Li W, Cheng X, Guo L, et al. Association between serum 25-hydroxyvitamin D concentration and pulmonary infection in children[J]. Medicine (Baltimore), 2018, 97(1): e9060

[6] Ekiz T, Yeğen SF, Katar MK, et al. 25-Hydroxyvitamin D levels and bone mineral density evaluation in patients with cholecystectomy: a case-control study[J]. Arch Osteoporos, 2018, 13(1): 14

[7] Tamaki J, Iki M, Sato Y, et al. Total 25-hydroxyvitamin D levels predict fracture risk: results from the 15-year follow-up of the Japanese Population-based Osteoporosis (JPOS) Cohort Study[J]. Osteoporos Int, 2017, 28(6): 1903-1913

[8] Lee DY, Jee JH, Cho YY, et al. Serum 25-hydroxyvitamin D cutoffs for functional bone measures in postmenopausal osteoporosis[J]. Osteoporos Int, 2017, 28(4): 1377-1384

[9] Zhu K, Oddy WH, Holt P, et al. Tracking of vitamin D status from childhood to early adulthood and its association with peak bone mass [J]. Am J Clin Nutr, 2017, 106(1): 276-283

[10] Bao L, Chen M, Lei Y, et al. Association between vitamin D receptor BsmI polymorphism and bone mineral density in pediatric patients: A meta-analysis and systematic review of observational studies[J]. Medicine (Baltimore), 2017, 96(17): e6718

[11] Tseng MH, Huang SM, Lo FS, et al. Functional Analysis of VDR Gene Mutation R343H in A Child with Vitamin D-Resistant Rickets with Alopecia[J]. Sci Rep, 2017, 7(1): 15337

[12] Koçyiğit C, Çatlı G, İnce G, et al. Can Stoss Therapy Be Used in Children with Vitamin D Deficiency or Insufficiency without Rickets?[J]. J Clin Res Pediatr Endocrinol, 2017, 9(2): 150-155

[13] 吕成银,谈文峰,张缪佳,等.维生素 D 与自身免疫病[J].江苏医药, 2013, 39(13): 1563-1566

[14] Pekkinen M, Saarnio E, Viljakainen HT, et al. Vitamin D binding protein genotype is associated with serum 25-hydroxyvitamin D and PTH concentrations, as well as bone health in children and adolescents in Finland[J]. PLoS One, 2014, 9(1): 87292-89293

[15] Villa CR, Chen J, Wen B, et al. Maternal vitamin D beneficially programs metabolic, gut and bone health of mouse male offspring in an obesogenic environment [J]. Int J Obes (Lond), 2016, 40(12): 1875-1883

[16] Rooze S, Mathieu F, Claus W, et al. Effect of calcium and vitamin D on growth, rickets and Kashin-Beck disease in 0- to 5-year-old children in a rural area of central Tibet[J]. Trop Med Int Health,2016, 21(6): 768-775

[17] Rajakumar K, Holick MF, Moore CG, et al. Impact of seasonal flux on 25-hydroxyvitamin D and bone turnover in pre- and early pubertal youth[J]. Pediatr Int, 2014, 56(1): 35-42

[18] 柴少卿,艾荣,于少飞,等.支气管哮喘患儿血清 25 羟维生素 D3 水平对病情评估及临床转归的意义[J].现代生物医学进展, 2015, 15 (34): 6721-6724

[19] Hazell TJ, Pham TT, Jean-Philippe S, et al. Vitamin D status is associated with bone mineral density and bone mineral content in preschool-aged children[J]. J Clin Densitom, 2015, 18(1): 60-67

[20] Science M, Maguire JL, Russell ML, et al. Prevalence and predictors of low serum 25-hydroxyvitamin D levels in rural Canadian children [J]. Paediatr Child Health, 2017, 22(3): 125-129

[21] Acosta-Bendek BM, Sánchez-Majana LP, Fonseca-Galé J, et al. Serum 25-hydroxyvitamin D state in healthy children ten year minors old of Barranquilla metropolitan area[J]. Salud Publica Mex, 2017, 59 (6): 657-664

[22] Blakeley CE, Van Rompay MI, Schultz NS, et al. Relationship between muscle strength and dyslipidemia, serum 25 (OH)D, and weight status among diverse schoolchildren: a cross-sectional analysis [J]. BMC Pediatr, 2018, 18(1): 23

[23] Husmann C, Frank M, Schmidt B, et al. Low 25 (OH)-vitamin D concentrations are associated with emotional and behavioral problems in German children and adolescents [J]. PLoS One, 2017, 12(8): e0183091

[24] Barja-Fernández S, Aguilera CM, Martínez-Silva I, et al. 25-Hydroxyvitamin D levels of children are inversely related to adiposity assessed by body mass index [J]. J Physiol Biochem, 2018, 74(1): 111-118

[25] Garcia AH, Erler NS, Jaddoe VWV, et al. 25-hydroxyvitamin D concentrations during fetal life and bone health in children aged 6 years: a population-based prospective cohort study [J]. Lancet Diabetes Endocrinol, 2017, 5(5): 367-376

[26] Akkermans MD, Eussen SR, van der Horst-Graat JM, et al. A micronutrient-fortified young-child formula improves the iron and vitamin D status of healthy young European children: a randomized, double-blind controlled trial [J]. Am J Clin Nutr, 2017, 105(2): 391-399

[27] Roh YE, Kim BR, Choi WB, et al. Vitamin D deficiency in children aged 6 to 12 years: single center's experience in Busan[J]. Ann Pediatr Endocrinol Metab, 2016, 21(3): 149-154

[28] Yu X, Zhang J, Yan C, et al. Relationships between serum 25-hydroxyvitamin D and quantitative ultrasound bone mineral density in 0-6 year old children[J]. Bone, 2013, 53(1): 306-310

[29] 王丽敏,张雪玲,王文娟,等.佳木斯地区 6 岁以下儿童血清维生素 A、25- 羟基维生素 D、维生素 E 水平分析[J].检验医学, 2017, 32 (4): 276-279

[30] Gómez-Campos R, Andruske CL, Arruda M, et al. Proposed equations and reference values for calculating bone health in children and adolescent based on age and sex [J]. PLoS One, 2017, 12(7): e0181918