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25-(OH)D₃与糖尿病周围神经病变的相关性

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[摘要] 目的: 分析25-(OH)D₃与糖尿病周围神经病变(diabetic peripheral neuropathy, DPN)的相关性, 评价其在DPN中的诊断价值。方法: 选取2017年11月至2018年8月于柳州市人民医院内分泌科住院的2型糖尿病患者148例作为研究对象, 依据神经电生理(nerve electrophysiology, NET)检查结果分为DPN组与非DPN组。148例2型糖尿病患者血清25-(OH)D₃在10.81~43.09 nmol/L, 根据25-(OH)D₃四分位数, 将2型糖尿病患者分为4组, 即A组[25-(OH)D₃<13.82 nmol/L]、B组[13.82 nmol/L≤25-(OH)D₃<21.42 nmol/L]、C组[21.42 nmol/L≤25-(OH)D₃<34.91 nmol/L]、D组[25-(OH)D₃≥34.91 nmol/L]。分析各组血清25-(OH)D₃水平, 神经运动神经传导速度(motor nerve conduction velocity, MCV)、腓肠感觉神经传导速度(sensory nerve conduction velocity, SCV)、神经F波潜伏期、运动传导波幅变化。结果: DPN组、非DPN组25-(OH)D₃水平分别为(35.08±2.89)nmol/L, (41.24±3.42)nmol/L, 组间比较差异具有统计学意义(P<0.05); 运动传导波幅在A组、B组、C组及D组四组中两两比较, 差异均具有统计学意义(P<0.05); A组神经潜伏期明显高于其他3组, 腓肠神经SCV明显低于其他3组, 差异有统计学意义(P<0.05); B组与C组神经潜伏期明显高于D组(P<0.05)。A组、B组、C组及D组DPN发生率分别为86.49%, 54.05%, 48.65%及27.03%, A组、B组和C组DPN发生率明显高于D组(P<0.05); B组和C组DPN发生率明显高于D组(P<0.05)。受试者工作特征(receiver operating characteristic, ROC)分析结果显示血清25-(OH)D₃水平诊断DPN曲线下面积(area under the curve, AUC)为0.642 (95%CI 0.581~0.796), 最佳临界诊断值为13.45 nmol/L。结论: 血清25-(OH)D₃水平可作为预测DPN程度的指标。

[关键词] 2型糖尿病; 周围神经病变; 25-(OH)D₃

25-(OH)D₃ and diabetic peripheral neuropathy

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Abstract **Objective:** To analyze the correlation between 25-(OH)D₃ and diabetic peripheral neuropathy (DPN) and evaluate its diagnostic value in DPN. **Methods:** A total of 148 patients with type 2 diabetes admitted to the Endocrinology Department of Liuzhou People's Hospital from November 2017 to August 2018 were selected as the research objects. According to the results of nerve electrophysiology (NET) examination,

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the patients were divided into DPN group and non-DPN group. Serum 25-(OH)₃D₃ of 148 patients with type 2 diabetes was at 10.81–43.09 nmol/L. According to the quartile of 25-(OH)₃D₃, type 2 diabetes patients were divided into four groups: Group A[25-(OH)₃D₃ <13.82 nmol/L], group B[13.82 nmol/L ≤ 25-(OH)₃D₃ <21.42 nmol/L], group C[21.42 nmol/L ≤ 25-(OH)₃D₃ <34.91 nmol/L], group D[25-(OH)₃D₃ ≥ 34.91 nmol/L], and then analyze the serum 25-(OH)₃D₃ level, median nerve MCV, sural nerve SCV, median nerve F wave latency, motion conduction amplitude changes. **Results:** The levels of 25-(OH)₃D₃ in the DPN group and non-DPN group were (35.08±2.89) nmol/L and (41.24±3.42) nmol/L, respectively. Pairwise comparison of motion conduction amplitude in group A, group B, group C and group D showed statistical significance ($P<0.05$). The latency of median nerve in group A was significantly higher than that of the other three groups, and the SCV of sural nerve was significantly lower than that of the other three groups, with statistical significance ($P<0.05$). The latency of median nerve in group B and group C was significantly higher than that in group D, with statistical significance ($P<0.05$). The DPN incidence in group A, group B, group C and group D was 86.49%, 54.05%, 48.65% and 27.03%, respectively. The DPN incidence in group A, group B and group C was significantly higher than that in group D, with statistical significance ($P<0.05$). DPN incidence in group B and group C was significantly higher than that in group D, with statistical significance ($P<0.05$). Receiver operating characteristic (ROC) analysis showed that the area under curve (AUC) of DPN diagnosed at serum 25-(OH)₃D₃ level was 0.642 (95% CI 0.581–0.796), and the optimal critical diagnostic value was 13.45 nmol/L. **Conclusion:** Serum 25-(OH)₃D₃ level can be used as an indicator to predict the degree of DPN.

Keywords type 2 diabetes mellitus; peripheral neuropathy; 25-(OH)₃D₃

糖尿病为临床常见慢性病, 据统计^[1-2], 2015年全球糖尿病患者达到4.15亿, 其中60%~70%伴随有糖尿病神经病变, 临床表现为四肢麻木、感觉过敏、心血管交感神经系统异常等, 严重影响患者的生命质量。糖尿病神经病变最为常见的是糖尿病周围神经病变(diabetic peripheral neuropathy, DPN), DPN发病机制尚不清楚, 但多数学者^[3-4]认为其发生发展和氧化应激、自身免疫、代谢异常等有关。维生素D作为胆固醇衍生物, 主要参与机体的钙磷代谢, 其能够与维生素D受体(vitamin D receptor, VDR)结合调节基因转录来发挥生物学效应^[5], 因此维生素D不仅局限于对钙磷代谢调节, 还参与细胞生长、分化以及免疫应答等。还有学者^[6]通过动物实验研究发现25-(OH)₃D₃对糖尿病大鼠神经具有保护作用, 但其与DPN的关系鲜有报道。本研究探讨25-(OH)₃D₃与DPN的相关性研究, 旨在为预防和治疗DPN提供数据支撑。

1 对象与方法

1.1 对象

选取2017年11月至2018年8月于柳州市人民医院内分泌科就诊的2型糖尿病患者作为研究对

象, 纳入标准: 患者均符合《中国2型糖尿病防治指南》(2015版)中的2型糖尿病诊断标准^[7]。排除标准: 1)伴严重肝肾功能障碍者; 2)伴其他内分泌疾病、感染、恶性肿瘤、自身免疫疾病、糖尿病急性并发症等者; 3)长期饮酒者; 4)因颈椎或脑血管病等原因引起的周围神经病变者。最终共纳入符合要求的患者148例, 148例2型糖尿病患者血清25-(OH)₃D₃在10.81~43.09 nmol/L范围内, 根据25-(OH)₃D₃四分位数, 将2型糖尿病患者分为4组: A组[25-(OH)₃D₃ <13.82 nmol/L]、B组[13.82 nmol/L ≤ 25-(OH)₃D₃ <21.42 nmol/L]、C组[21.42 nmol/L ≤ 25-(OH)₃D₃ <34.91 nmol/L]、D组[25-(OH)₃D₃ ≥ 34.91 nmol/L]。对患者进行神经电生理(nerve electrophysiology, NET)检查, 周围神经病变诊断标准参照《临床肌电图学》^[8], 将未合并有DPN的患者68例作为非DPN组, 其中男46例, 女22例, 年龄(54.19±10.92)岁, 病程(3.49±1.18)年; 余下80例伴随有DPN的患者作为DPN组, 其中男52例, 女28例, 年龄(54.45±10.86)岁, 病程(3.53±1.22)年。经统计学分析, 两组基本资料无统计学意义($P>0.05$)。本研究经柳州市人民医院医学伦理委员会审核批准, 患者均签署知情同意书。

1.2 方法

1.2.1 血清 25-(OH)D₃ 检测

入院后3 d内禁止患者饮用咖啡、茶水等饮料, 避免进行剧烈运动, 于清晨空腹抽取肘静脉血5 mL, 离心获得血清, 采用电化学发光仪检测25-(OH)D₃。

1.2.2 NET 检查

患者取平卧位, 室温23~25 ℃, 用热水袋保持体表温度在34~36 ℃, 然后采用Nicolet Viking Select肌电诱发电位仪分别行神经运动神经传导速度(motor nerve conduction velocity, MCV)、感觉神经传导速度(sensory nerve conduction velocity, SCV)、神经F波潜伏期、运动传导波幅检测。本研究均由同一位经验丰富的肌电图专业人员进行操作。

1.3 统计学处理

采用SPSS 16.0统计软件进行数据分析, 符合正态分布的计量资料采用均数±标准差($\bar{x} \pm s$)进行表示, 多组间比较采用单因素方差分析, 两两比较采用 t 检验, 分类资料采用率表示, 组间比较 χ^2 采用检验。绘制受试者工作特征(receiver operating characteristic, ROC)曲线观察25-(OH)D₃在DPN中的诊断价值, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 DPN组与非DPN组血清25-(OH)D₃水平对比

DPN组与非DPN组25-(OH)D₃水平分别为(35.08±2.89)nmol/L与(41.24±3.42)nmol/L, DPN组25-(OH)D₃水平明显低于非DPN组, 差异有统计学意义($P < 0.05$)。

2.2 不同血清25-(OH)D₃水平周围神经病变指标比较

分析神经MCV、腓肠神经SCV、神经F波潜伏期、运动传导波幅变化, 结果显示: 运动传导波幅在4组中两两比较, 差异均有统计学意义($P < 0.05$); A组神经潜伏期明显高于其他3组, 腓肠神经SCV明显低于其他3组, 差异有统计学意义($P < 0.05$); B组和C组神经潜伏期明显高于D组, 差异有统计学意义($P < 0.05$, 表1)。

2.3 不同血清25-(OH)D₃水平周围神经病变患者比较

A组、B组和C组DPN发生率明显高于D组, 差异有统计学意义($P < 0.05$); B组和C组DPN发生率明显高于D组, 差异有统计学意义($P < 0.05$, 表2)。

表1 不同血清25-(OH)D₃水平周围神经病变指标比较($n=37$)

Table 1 Comparison of peripheral neuropathy indicators in different serum levels of 25-(OH)D₃ ($n=37$)

组别	运动传导波幅	神经 MCV/(m·s ⁻¹)	神经 F 波潜伏期/(m·s ⁻¹)	腓肠神经 SCV/(m·s ⁻¹)
A 组	6.28 ± 0.79 ^{*#&}	56.71 ± 6.42	3.61 ± 0.43 ^{*#&}	47.92 ± 6.53 ^{*#&}
B 组	6.72 ± 0.87 ^{*#}	56.82 ± 6.38	3.39 ± 0.58 [*]	52.88 ± 7.09
C 组	7.31 ± 0.92 [*]	56.39 ± 6.25	3.43 ± 0.61 [*]	52.79 ± 7.11
D 组	7.91 ± 0.85	57.04 ± 6.54	3.09 ± 0.56	52.49 ± 6.98

与D组对比, ^{*} $P < 0.05$, 与C组对比, [#] $P < 0.05$, 与B组相比, [&] $P < 0.05$ 。

Compared with group D, ^{*} $P < 0.05$; compared with group C, [#] $P < 0.05$; compared with group B, [&] $P < 0.05$.

表2 不同血清25-(OH)D₃水平周围神经病变指标比较($n=37$)

Table 2 Comparison of peripheral neuropathy indicators in different serum levels of 25-(OH)D₃ ($n=37$)

组别	非 DPN	DPN	DPN 发生率/%
A 组	27	10	27.03
B 组	19	18	48.65 [*]
C 组	17	20	54.05 [*]
D 组	5	32	86.49 ^{*#&}

与D组对比, ^{*} $P < 0.05$, 与C组对比, [#] $P < 0.05$, 与B组相比, [&] $P < 0.05$ 。

Compared with group D, ^{*} $P < 0.05$; compared with group C, [#] $P < 0.05$; compared with group B, [&] $P < 0.05$.

2.4 血清 25-(OH)D₃ 水平在 DPN 中的诊断价值

经 ROC 分析, 血清 25-(OH)D₃ 水平诊断 DPN 曲线下面积 (area under the curve, AUC) 为 0.642 (95% CI 0.581~0.796), 最佳临界诊断值为 13.45 nmol/L (图 1)。

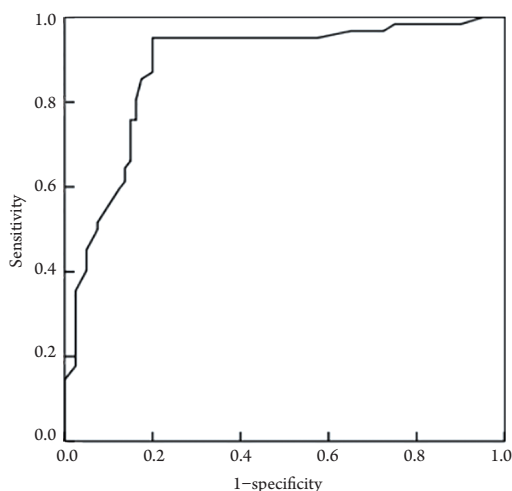


图 1 ROC 曲线预测血清 25-(OH)D₃ 水平在 DPN 中的诊断价值
Figure 1 Diagnostic value of serum 25-(OH)D₃ level in DPN by ROC curve

3 讨论

维生素 D 作为脂溶性维生素, 主要以 25-(OH)D₃ 形式存在于人体内, 不仅可以调节钙磷代谢, 还对细胞生长、分化以及免疫应答、胰岛素分泌等具有调节作用^[9]。大量数据^[10-11]显示维生素 D 缺乏和糖尿病发病有关。糖尿病最为常见的慢性并发症为 DPN, 其能对患者的神经功能造成严重损害, 引起感知功能丧失, 致残率极高。近些年来, 随着生活水平的不断提高, 饮食结构发生变化, 糖尿病发病率呈逐年递增趋势, DPN 发病人数也在不断增加, 给患者及其家庭带来严重的经济和精神负担, 因此如何早期诊治 DPN 成为医学工作者不断探寻的课题。

提升 DPN 早期筛查率、及时确诊、指导临床有效防治, 是降低 DPN 对患者造成功能损害、优化预后、提升患者生活质量的关键, 但 DPN 早期没有特异性症状, 因此很难尽早确诊, 患者在就诊时往往错过了最佳治疗时机。大量研究^[12-13]证实: 25-(OH)D₃ 与心血管疾病、肾病、视网膜病变等有明显相关性。25-(OH)D₃ 主要与 VDR 结合发挥生物学作用。有学者^[14]发现: VDR 不仅存在骨骼

肌、肾脏以及肠道组织中, 还存在与免疫系统、内分泌系统中。多数学者^[15-16]认为糖尿病神经病变和血清 25-(OH)D₃ 密切相关。汤孝优等^[17]纳入 207 例糖尿病患者, 其中 DPN 患者 128 例, 对三酰甘油、胆固醇、C 反应蛋白等进行单因素和 logistic 回归分析, 结果显示 25-(OH)D₃ 是引起糖尿病神经病变的高危因素。还有学者^[18]将心电图、神经自觉症状等检查结果进行分析, 发现 25-(OH)D₃ 在 DPN 过程中具有预测作用, 表明 25-(OH)D₃ 缺乏会影响胰岛素分泌, 增加胰岛素抵抗, 使机体处于高糖应激状态, 从而使神经细胞脱髓鞘反应加速神经病变发生。本研究对不同血清 25-(OH)D₃ 水平周围神经病变指标进行测定发现: 随着血清 25-(OH)D₃ 水平升高, 运动传导波幅、腓肠神经 SCV 明显升高, 而神经潜伏期明显缩短, 同时伴随着 25-(OH)D₃ 水平升高, 周围神经病变的发生率也明显降低。本研究还进一步采用 ROC 曲线预测血清 25-(OH)D₃ 水平在 DPN 中的诊断价值, 结果显示当血清 25-(OH)D₃ 水平 < 13.45 nmol/L 时, 神经病变发生概率增高。

综上, 血清 25-(OH)D₃ 水平在 DPN 患者中呈现低表达, 与运动传导波幅、腓肠神经 SCV 及神经潜伏期均有关系, 可作为预测 DPN 程度的指标。

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