

doi: 10.13241/j.cnki.pmb.2015.17.033

甲状旁腺激素及血清钙水平与脓毒症患者病情严重程度和预后的关系

朱永麦 叶吴远怡 陈明科 李瑞

(海南省人民医院重症医学科 海南 海口 570311)

摘要 目的:探究甲状旁腺激素(PTH)及血清钙(Ca)水平与脓毒症患者病情严重程度和预后的关系。**方法:**选取2010年9月至2014年2月我收治的80例脓毒症患者,根据存活情况分为存活组(38例)和死亡组(42例),根据血Ca水平分为正常血钙组(32例)和低血钙组(48例)。检测患者PTH、Ca水平,采用急性生理和慢性健康评分(APACHE II)评价患者病情严重程度,分析APACHE II评分与PTH、Ca水平的相关性,以及Ca水平与预后的关系。**结果:**生存组PTH水平及APACHE II评分均低于死亡组,血Ca水平高于死亡组,差异均具有统计学意义($P<0.05$);APACHE II评分与血Ca呈负相关($r=-0.581, P<0.05$),与PTH水平呈明显正相关($r=0.423, P<0.05$);正常血钙组治疗后死亡率为25.00%(8/32),低于低血钙组的66.67%(32/48),差异有统计学意义($\chi^2=13.333, P<0.05$)。**结论:**PTH及Ca水平与脓毒症重症患者病情严重程度有显著关系,低血Ca提示患者预后差。

关键词: 甲状旁腺激素;血清钙;APACHE II评分;脓毒症

中图分类号: R631.2 **文献标识码:** A **文章编号:** 1673-6273(2015)17-3319-03

Relationship Between Parathyroid Hormone, Serum Calcium and Disease Severity, Prognosis of Sepsis Patients

ZHU Yong, MAI Ye, WU Yuan-yi, CHEN Ming-ke, LI Rui

(Department of ICU, Hainan Provincial People's Hospital, Haikou, Hainan, 570311, China)

ABSTRACT Objective: To explore the relationship between parathyroid hormone (PTH), serum calcium (Ca) and disease severity, prognosis of sepsis patients. **Methods:** 80 cases of sepsis patients were treated in our hospital between September 2010 and February 2010, which were divided into survival group (38 cases) and death group (42 cases) according to the survival situation, and were divided into normal calcium group (32 cases) and low calcium group (48 cases) according to the Ca level. The PTH and serum Ca level were detected, the disease severity was evaluated using the acute physiology and chronic health score (APACHE II). Analyzed the correlation between APACHE II score and PTH, serum Ca level, and the relationship between Ca level and prognosis. **Results:** The PTH level and APACHE II score of the survival group was lower than that in death the group, the serum Ca level was higher than that of death group, the difference was statistically significant ($P<0.05$); APACHE II score was negatively correlated with serum Ca ($r=-0.581, P<0.05$), while positively correlated with the PTH level ($r=0.423, P<0.05$); After treatment, the mortality rate of normal calcium group was 25% (8/32), lower than 66.67% (32/48) in the low calcium group, the difference was statistically significant ($\chi^2=13.333, P<0.05$). **Conclusion:** There is a significant relationship between serum PTH and Ca level and disease severity of sepsis patients, and Low serum Ca indicates a poor prognosis.

Key words: Parathyroid hormone; Serum calcium; APACHE II score; Sepsis

Chinese Library Classification(CLC): R631.2 **Document code:** A

Article ID: 1673-6273(2015)17-3319-03

前言

脓毒症(Sepsis)是一种全身炎症反应综合征(Systemic inflammatory response syndrome, SIRS),主要是因细菌造成的全身性感染,甚至导致机体内多器官功能衰竭(multiple organ failure, MOF)^[1,2]。在全球范围内,危重病患者发展成脓毒症概率逐渐增加,脓毒症成为ICU中患者死亡的主要死因^[3]。有研究显示,新增脓毒症患者每年75万例,脓毒症休克占75%,病死率

高达35%以上^[4]。SIRS、脓毒症或是MOF等常引起机体内严重的应激状态,导致患者机体内出现神经、内分泌紊乱,机体外周血内应激激素分泌量大大增加,如胰高血糖、皮质醇、肾上腺素等,导致患者内环境稳态打破,常见表现为电解质浓度异常,血钙(calcium, Ca)水平异常^[5-7]。正常机体内含量最高的一类矿物质是钙,且钙离子可用作细胞内传递信息的第二信使,调节机体细胞内各种生理功能^[8,9],因此钙离子一旦浓度异常,对上述细胞功能造成严重影响,难以正常维持细胞结构和功能,而脓毒症患者常出现机体内分泌代谢紊乱,生理功能异常^[10]。甲状旁腺激素(parathyroid hormone, PTH)是一种无激素活性物质,降钙素前体^[11]。本文通过检测80例ICU脓毒症患者机体内血

作者简介:朱永(1967-),男,本科,副主任医师,从事重症医学方面的研究, E-mail: zhuyong22333@126.com

(收稿日期:2015-01-05 接受日期:2015-01-28)

Ca、PTH 水平以探究其与脓毒症患者病情严重程度以及患者预后间的相互关系,现将研究内容报道如下:

1 资料与方法

1.1 临床资料

回顾性分析 2010 年 9 月至 2014 年 2 月我院收治的脓毒症 80 例患者的临床资料,纳入标准为:患者均符合 2001 年 SCCM/ESICM/ACCP/ATS/SIS 联席会议有关脓毒症诊断标准^[12],经患者及家属知情同意。排除标准:合并其他可导致机体内 PTH、血 Ca 浓度增加疾病患者,如慢性肝肾功能不全、恶性肿瘤、胃肠手术、糖尿病、甲状旁腺疾病、骨病、重症胰腺炎,或是患者近期内曾进行钙剂治疗者。根据研究期间患者存活情况将其分为存活组(38 例)和死亡组(42 例),存活组男 24 例,女 14 例,平均年龄(65.6±4.5)岁;死亡组男 26 例,女 16 例,平均年龄(66.1±4.7)岁。两组患者年龄及性别比差异无统计学意义($P>0.05$)。根据血钙水平分为正常血钙组 32 例,低血钙组 48 例。

1.2 标本处理方法

① PTH 采集和处理:选择无肝素试管,采集患者静脉血备

用。血标本采集后,经 30-60 min 室温下放置,随后进行 2500 r/min 离心 10 min。静置后于 -70℃ 下保存;采用免疫发光法检测,PTH 正常上限为 55 ng/L;② 血 Ca 水平测定:选择有肝素试管采集患者静脉血,自动分析仪检测,血 Ca 正常范围为 2.1-2.6 mmol/L。

1.3 观察指标

每日监测患者机体内血 Ca、PTH 水平,并进行急性生理和慢性健康评分(APACHE II)^[9],分析 APACHE II 评分与 PTH、Ca 水平的相关性。

1.4 统计学处理

采用 SPSS18.0 软件进行统计分析,计数资料组间行 t 检验。APACHE II 评分与血 Ca、PTH 水平的相关性采用 spearman 关系分析, $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 生存组和死亡组 PTH、Ca 水平和 APACHE II 评分比较

生存组 PTH 水平和 APACHE II 评分低于死亡组,血 Ca 浓度高于死亡组,差异均统计学意义($P<0.05$),见表 1。

表 1 两组 PTH、Ca 水平和 APACHE II 评分比较($\bar{x} \pm s$)

Table 1 Comparison of PTH, Ca level and APACHE II score between two groups($\bar{x} \pm s$)

指标 Indexes	存活组 Survival group	死亡组 Death group	t	P
APACHE II	18.6±3.2	31.2±4.1	-15.209	0.000
PTH(pmol/L)	6.17±2.8	9.62±3.3	-5.015	0.000
Ca(mmol/L)	1.14±0.07	0.93±0.08	12.436	0.000

2.2 APACHEII 评分与血 Ca、PTH 关系分析

APACHEII 评分与血 Ca 呈负相关($r=-0.581$, $P<0.05$)、与 PTH 水平呈明显正相关($r=0.423$, $P<0.05$)。

2.3 血 Ca 与预后关系

正常血钙组治疗后死亡率为 25.00%(8/32),低于低血钙组的 66.67%(32/48),差异有统计学意义($\chi^2=13.333$, $P<0.05$)。

3 讨论

脓毒症是一种危重疾病,已经成为医学研究热点,主要因细菌造成的全身性感染。近年来,随着研究逐渐深入,基础医学发展,医学领域对脓毒症生理、生化以及免疫病理等方面有更加细致的了解。SIRS、脓毒症或 MOF 能引起机体内严重的应激状态,机体处于应激状态时,脓毒症患者常出现神经内分泌代谢紊乱症状,其主要临床表现为血清游离钙在内的电解质分泌紊乱^[13]。国外动物研究实验结果显示^[14],患有脓毒症的马易出现机体内血 Ca 水平调节紊乱,且死亡率较高,血 Ca 调节紊乱与死亡率呈显著相关关系;患有脓毒症的狗在进行血培养后,出现阳性病例出现低钙血症发生比率更高。

本研究发现血生存组 Ca 水平高于死亡组,差异均统计学意义($P<0.05$),正常血钙组治疗后死亡率为 25.00%(8/32),低于低血钙组的 66.67%(32/48),差异有统计学意义($\chi^2=13.333$,

$P<0.05$)。结合相关研究,低钙血症出现的原因存主要有:①骨钙动员及重吸收障碍:脓毒症常合并低镁血症,抑制 PTH 分泌,因此在机体内肾小管和骨骼等处对 PTH 敏感度下降,造成钙流失^[15];②降钙素释放,骨吸收抑制:脓毒症患者早期分泌胰高血糖素量提高,释放降钙素,骨吸收钙量下降^[16];③白蛋白分解,血钙流失:机体内血清内钙离子运载依靠白蛋白,脓毒症患者机体内胰高血糖素、儿茶酚胺分泌量提高,分解蛋白质,微血管对白蛋白通透性提高,因此钙离子穿过血管,聚集在组织间隙^[17];④脓毒血症患者机体内出现大量细胞因子,对依赖型钙通道显著激活,导致机体内 Ca^{+} 内流,细胞内 Ca^{+} 浓度增加,细胞内钙浓度增加^[18];⑤脓毒症患者住院治疗时,进食少,很少接触日光照射,胃肠道功能损害也使得钙吸收下降,维生素 D 吸收利用削弱,对血钙浓度存在抑制作用。因此血 Ca 与脓毒症患者有密切关系,影响患者预后。

生存组 PTH 水平及 APACHE II 评分均低于死亡组,APACHEII 评分与血 Ca 呈负相关,与 PTH 水平呈明显正相关。提示 PTH 水平与脓毒症患者的病情有关系,低 PTH 水平影响患者生存状况。可能原因:①脓毒症患者 PTH 对钙传感功能存在障碍,甲状旁腺细胞内钙浓度改变,导致分泌 PTH 浓度改变。PTH 对骨作用减轻,PTH 浓度增加,血钙水平并未升高^[18]。

②脓毒症患者机体内儿茶酚胺常常保持较高水平,对PTH水平存在影响,可能因为血液循环中血Ca水平降低,PTH分泌水平受儿茶酚胺直接影响^[19];③脓毒症患者常表现出显著低镁血症、炎症反应的临床特征,低镁血症对分泌PTH可能会造成损害^[20]。

综上所述,PTH异常与低钙血症是脓毒症患者中常见的症状,与患者病情严重程度及预后存在显著相关性。因此,检测脓毒血症患者进行PTH、血Ca水平对判断患者病情发展及预后存在重要作用。

参考文献(References)

- [1] 林勇军,熊滨,吕立文,等.小剂量氢化可的松治疗脓毒症休克临床研究[J].广西医学,2011,33(6):653-656
Lin Yong-jun, Xiong Bin, Lv Li-wen, et al. Clinical study of small dose of hydrocortisone for treatment of septic shock [J]. Guangxi medicine, 2011, 33(6): 653-656
- [2] Xiang J, Guan SD, Song XH, et al. Negative modulation of NO for diaphragmatic contractile reduction induced by sepsis and restraint position[J]. Journal of Forensic Medicine, 2014, 30(3): 161-165
- [3] Neamatzadeh H. Risk of postoperative hypocalcemia in patients underwent total thyroidectomy, subtotal thyroidectomy and lobectomy surgeries[J]. Acta Med Iran, 2014, 52(3): 206-209
- [4] Kaynar AM, Yende S, Zhu L, Frederick DR, et al. Effects of intra-abdominal sepsis on atherosclerosis in mice[J]. Crit Care, 2014, 18(5): 469
- [5] Harb A, Smith O, Lloyd H, et al. A case of fulminant portal pyemia complicating hemicolectomy for polyps: literature review and case report[J]. J Gastrointest Surg, 2010, 14(5): 926-928
- [6] Watanabe H, Mishima K, Uchida M, et al. Time Course of Calcium Concentrations and Risk Factors for Hypocalcemia in Patients Receiving Denosumab for the Treatment of Bone Metastases From Cancer[J]. Ann Pharmacother, 2014, 48(9): 1159-1165
- [7] Leone M, Bechis C, Baumstarck K, et al. De-escalation versus continuation of empirical antimicrobial treatment in severe sepsis: a multicenter non-blinded randomized noninferiority trial [J]. Intensive Care Med, 2014, 40(10): 1399-1408
- [8] Rajapakse S, Ranasinghe P, Parthithipan B, et al. Hypocalcemia is associated with disease severity in patients with dengue [J]. J Infect Dev Ctries, 2014, 8(9): 1205-1209
- [9] Cavaco B, Leite V. Chronic hypocalcemia due to anti-calcium sensing receptor antibodies[J]. Acta Med Port, 2014, 27(3): 399-402
- [10] Tasoglu O, Ordu-Gokkaya NK, Yenigun D, et al. Spasticity with hypocalcemia: Does spasticity have a metabolic determinant [J]. J Rehabil Med, 2014, 46(9): 941
- [11] Celes MR, Malvestio LM, Suadican SO, et al. Disruption of calcium homeostasis in cardiomyocytes underlies cardiac structural and functional changes in severe sepsis[J]. PLoS One, 2013, 8(7): e68809
- [12] Wu J, Zhang YY, Feng DG, et al. Changes of thyroxine and monocyte human leukocyte antigen-DR expression in senior patients with sepsis [J]. Journal of Southern Medical University, 2010, 30(1): 143-145
- [13] Payne R, Tabah R. Parathyroid hormone levels 1 hour after thyroidectomy: an early predictor of postoperative hypocalcemia[J]. Can J Surg, 2014, 57(4): 237-240
- [14] Yadav S, Yadav YS, Goel MM, et al. Calcitonin gene-and parathyroid hormone-related peptides in normotensive and preeclamptic pregnancies: a nested case-control study [J]. Arch Gynecol Obstet, 2014, 290(5): 897-903
- [15] Neamatzadeh H. Risk of postoperative hypocalcemia in patients underwent total thyroidectomy, subtotal thyroidectomy and lobectomy surgeries[J]. Acta Med Iran, 2014, 52(3): 206-209
- [16] Bouillet L, Casez O. Severe acute neurological symptoms related to proton pump inhibitors induced hypomagnesemia responsible for profound hypoparathyroidism with hypocalcemia [J]. Clin Res Hepatol Gastroenterol, 2014, 10: 1016
- [17] Pinheiro da Silva F, Zampieri FG, Barbeiro HV, et al. Decreased parathyroid hormone levels despite persistent hypocalcemia in patients with kidney failure recovering from septic shock [J]. Endocr Metab Immune Disord Drug Targets, 2013, 13(2): 135-142
- [18] Koesters A, Engisch KL, Rich MM. Decreased cardiac excitability secondary to reduction of sodium current may be a significant contributor to reduced contractility in a rat model of sepsis [J]. Crit Care, 2014, 18(2): R54
- [19] Ikeda S, Yamamoto H, Masuda M, et al. Downregulation of renal type IIa sodium-dependent phosphate cotransporter during lipopolysaccharide-induced acute inflammation [J]. Am J Physiol Renal Physiol, 2014, 306(7): F744-750
- [20] Hu G, Peng Y, Wang F, et al. Effects of blood purification in the treatment of patients with burn sepsis [J]. Chinese Journal of Burns, 2014, 30(3): 213-218
- [17] Jia S, Wang F, Li F, et al. Rapid detection of hepatitis B virus variants associated with lamivudine and adefovir resistance by multiplex ligation-dependent probe amplification combined with real-time PCR [J]. J Clin Microbiol, 2014, 52(2): 460-466
- [18] Maier M, Liebert UG, Wittekind C, et al. Clinical Relevance of Minimal Residual Viremia during Long-Term Therapy with Nucleos(t)ide Analogues in Patients with Chronic Hepatitis B [J]. PLoS One, 2013, 8(6): e67481
- [19] Lavocat F, Dény P, Pichoud C, et al. Similar evolution of hepatitis B virus quasispecies in patients with incomplete adefovir response receiving tenofovir/ emtricitabine combination or tenofovir monotherapy[J]. J Hepatol, 2013, 59(4): 684-695
- [20] Rodriguez C, Chevalier S, Bensadoun P, et al. Characterization of the dynamics of hepatitis B virus resistance to adefovir by ultra-deep pyrosequencing[J]. Hepatology, 2013, 58(3): 890-901

(上接第 3282 页)