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术前白蛋白水平对继发性甲状旁腺功能亢进患者术后 重度低钙血症的预测价值

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[摘要] 目的: 探讨术前白蛋白(albumin, ALB)水平对继发性甲状旁腺功能亢进(secondary hyperthyroidism, SHPT)患者术后重度低钙血症(severe hypocalcemia, SH)的预测价值。方法: 回顾性分析2019年1月至2021年6月六安市中医院甲乳外科收治90例SHPT患者的相关资料, 依据甲状旁腺切除术(parathyroidectomy, PTX)术后血钙监测情况, 分为SH组(血钙水平 ≤ 1.8 mmol/L; $n=29$)与对照组(血钙水平 > 1.8 mmol/L, $n=61$)。比较两组围手术期相关资料, 采用多因素logistic回归模型和绘制受试者工作特征(receiver operating characteristic, ROC)曲线分析术前ALB水平与SHPT患者PTX术后SH发生的关系。结果: SH组术前碱性磷酸酶(alkaline phosphatase, ALP)、ALB水平和甲状旁腺切除个数 ≥ 4 个的比重高于对照组($P < 0.05$)。术前ALP(OR=1.442, 95%CI: 1.334~5.881)、术前ALB(OR=1.391, 95%CI: 1.168~3.159)、甲状旁腺切除数 ≥ 4 个(OR=2.248, 95%CI: 1.211~7.352)是PTX术后SH发生的独立危险因素($P < 0.05$)。术前ALB预测SHPT患者PTX术后SH发生的曲线下面积(area under curve, AUC)为0.714(95%CI: 0.577~0.850), 术前ALP预测的ACU为0.729(95%CI: 0.586~0.872), 二者比较差异无统计学意义($P > 0.05$)。结论: 术前ALB水平是SHPT患者PTX术后SH发生的危险因素, 对临床早期筛查SH高危人群和预测SH发生有参考价值。

[关键词] 继发性甲状旁腺功能亢进; 甲状旁腺切除术; 白蛋白; 重度低钙血症; 预测

Value of preoperative albumin level in predicting postoperative severe hypocalcemia in patients with secondary hyperparathyroidism

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Abstract **Objective:** To investigate the predictive value of preoperative albumin (ALB) level on postoperative severe hypocalcemia (SH) in patients with secondary hyperparathyroidism (SHPT). **Methods:** The data of 90 patients with SHPT treated in the Department of Thyroid Gland and Breast Surgery of Lu'an Hospital of Traditional Chinese Medicine from January 2019 to June 2021 were analyzed retrospectively. According to the

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blood calcium monitoring after parathyroidectomy (PTX), they were divided into an SH group (blood calcium level ≤ 1.8 mmol/L, $n=29$) and a control group (blood calcium level >1.8 mmol/L, $n=61$). The perioperative related data of the 2 groups were compared. The relationship between preoperative ALB level and the occurrence of SH after PTX in SHPT patients was analyzed by multivariate logistic regression model and receiver operating characteristic curve. **Results:** The levels of alkaline phosphatase (ALP), ALB, and the proportion of parathyroid resection ≥ 4 in SH group were significantly higher than those in the control group ($P<0.05$). Preoperative ALP (OR = 1.442, 95%CI: 1.334–5.881), preoperative ALB (OR = 1.391, 95%CI: 1.168–3.159) and the number of parathyroidectomy ≥ 4 (OR = 2.248, 95%CI: 1.211–7.352) were independent risk factors for SH after PTX ($P<0.05$). The area under curve (AUC) predicted by preoperative ALB was 0.714 (95%CI: 0.577–0.850), and ACU predicted by preoperative ALP was 0.729 (95%CI: 0.586–0.872), without significant difference between the 2 groups ($P>0.05$). **Conclusion:** Preoperative ALB level is a risk factor for SH after PTX in SHPT patients. It has reference value for early screening high-risk groups of SH and predicting the occurrence of SH.

Keywords secondary hyperparathyroidism; parathyroidectomy; albumin; severe hypocalcemia; prediction

低钙血症是继发性甲状腺功能亢进(secondary hyperthyroidism, SHPT)手术患者的常见并发症, 发生率可达75%~90%^[1], SH可引起患者抽搐、心率失常、癫痫甚至猝死等不良后果。因此在加强甲状旁腺切除术(parathyroidectomy, PTX)术后血钙和生命体征监测前提下, 术前寻找可预测SHPT患者PTX术后发生重度低钙血症(severe hypocalcemia, SH)的指标具有重要意义。既往研究^[2-3]表明: 年龄、术前ALP、甲状旁腺切除数量是术后SH发生的危险因素。白蛋白(albumin, ALB)是血液循环中主要的钙结合蛋白, 与肝、肾脏器病变密切相关, 肾病综合征、甲亢患者常见血清ALB减低, 且低蛋白血症与肾脏疾病进展和预后存在紧密关系^[4-5], 笔者推测, 血清ALB水平与SHPT患者PTX术后SH的发生也存在某种关联, 术前血清ALB水平对临床筛查SH高危人群和预测SH发生风险的价值尚不明确, 相关报道也较缺乏。因此, 本研究回顾性分析90份病例资料, 探究术前ALB水平对SHPT患者PTX术后发生SH的预测价值。

1 对象与方法

1.1 对象

回顾性分析2019年1月至2021年6月在安徽省六安市中医院甲乳外科治疗的90例SHPT患者的相关资料。纳入标准: 1) 患者年龄 >18 岁, 有明显慢性肾功能不全病史; 2) 术前检查显示甲状旁腺素(parathyroid hormone, PTH) >800 pg/mL, 高血钙和/或高血磷水平, 主诉有骨痛、肌无力或皮肤瘙痒等症状; 3) 患者既往药物治疗无效, 均自愿接

受并完成PTX治疗, 手术在多学科协作下完成, 且围手术期资料保留完整。排除标准: 术前相关检查资料和手术资料残缺者。本研究获六安市中医院医学伦理委员会审批。

1.2 方法

1.2.1 SH 诊断标准和分组方法

依据肾脏病后预后质量(Kidney Disease Outcomes Quality Initiative, KDOQI)指南, 血清总钙正常参考值范围为2.15~2.58 mmol/L, 若血钙水平 ≤ 1.8 mmol/L, 即可诊断为SH。本研究依据SHPT患者PTX术后血钙水平的监测情况, 分为SH组(血钙水平 ≤ 1.8 mmol/L, $n=29$)和对照组(血钙水平 >1.8 mmol/L, $n=61$), 分别占32.22%和67.78%。

1.2.2 资料收集

收集SH组和对照组下列围手术期资料: 性别、年龄、体重、临床表现(骨痛、皮肤瘙痒等)、透析年限、透析类型、术前检测指标[血钙、血磷、ALP、ALB、血红蛋白(hemoglobin, Hb)]、手术时间、出血量、甲状旁腺切除个数(≥ 4 个、 <4 个)等。其中术前检测指标均统计术前1 d的检测水平, 成人血清ALB水平正常参考值范围为35~55 g/L。

1.3 统计学处理

应用SPSS 21.0统计软件分析所得数据。计数资料用例(%)描述, 组间比较采用 χ^2 检验或Fisher确切概率法检验。计量资料经检验, 均满足正态分布和方差齐性并用均数 \pm 标准差($\bar{x}\pm s$)描述, 组间比较采用 t 检验。采用logistic回归模型进行多因素分析, 绘制受试者工作特征(receiver operating

characteristic, ROC)曲线评价相关指标对SHPT患者PTX术后发生SH的预测价值,曲线下面积(area under the curve, AUC)比较用秩和检验。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组 SHPT 患者相关资料比较

SH组和对对照组在性别、年龄、体重、临床表现、透析年限、透析类型、术前检测指标(血钙、血磷、Hb)、手术时间、出血量方面的比较,差异无统计学意义(均 $P > 0.05$)。SH组术前ALP、ALB水平和甲状旁腺切除数 ≥ 4 个的比重均高于对照组,差异有统计学意义($P < 0.05$ 或 $P < 0.001$,表1)。

2.2 SHPT 患者 PTX 术后发生 SH 的影响因素

将SHPT患者PTX术后是否发生SH作为因变

量,表1分析中有统计学意义的指标(术前ALP、术前ALB和甲状旁腺切除个数)以及从临床角度认为可能有意义的因素(术前血钙)进行逐步logistic回归分析。结果显示:术前ALP、ALB、甲状旁腺切除数 ≥ 4 个是SHPT患者PTX术后发生SH的独立危险因素($P < 0.05$,表2)。

2.3 术前 ALP、ALB 水平预测 SHPT 患者 PTX 术后发生 SH 的 ROC 曲线分析

将SHPT患者PTX术后是否发生SH作为状态变量(发生=1,未发生=0),将术前ALP、术前ALB水平绘制ROC曲线分析。结果显示:术前ALP、ALB水平对预测SHPT患者PTX术后发生SH的AUC均 > 0.7 ,分别为0.729、0.714,二者比较差异无统计学意义($Z = 1.206$, $P = 0.178$),二者最佳截断值分别为597.38 U/L、38.72 g/L(表3,图1)。

表1 两组SHPT患者相关资料比较

Table 1 Comparison of relevant data between the two groups of SHPT patients

资料	SH组(n=29)	对照组(n=61)	χ^2/t	P
男性/[例(%)]	13 (44.83)	30 (49.18)	0.149	0.699
年龄/岁	53.27 ± 11.58	54.06 ± 12.07	0.294	0.770
体重/kg	60.73 ± 10.25	61.02 ± 10.51	0.123	0.902
临床表现/[例(%)]				
骨痛	21 (72.41)	47 (77.05)	0.229	0.633
皮肤瘙痒	19 (65.52)	43 (70.49)	0.227	0.634
透析类型/[例(%)]			0.091	0.763
腹膜透析	7 (24.14)	13 (21.31)		
血液透析	22 (75.86)	48 (78.69)		
透析年限/年	6.72 ± 2.21	6.58 ± 2.15	0.286	0.776
术前血钙/(mmol·L ⁻¹)	2.47 ± 0.28	2.54 ± 0.31	1.032	0.305
术前血磷/(mmol·L ⁻¹)	1.98 ± 0.40	2.06 ± 0.37	0.934	0.353
术前ALP/(U·L ⁻¹)	751.23 ± 206.08	447.91 ± 124.25	8.680	<0.001
术前ALB/(g·L ⁻¹)	41.49 ± 4.27	35.60 ± 4.01	6.378	<0.001
术前Hb/(g·L ⁻¹)	107.29 ± 16.53	108.71 ± 15.97	0.395	0.694
手术时间/min	71.38 ± 15.07	70.46 ± 14.38	0.279	0.781
出血量/mL	28.71 ± 7.36	26.90 ± 7.24	1.103	0.273
甲状旁腺切除数/[例(%)]			5.092	0.024
≥ 4 个	22 (75.86)	31 (50.82)		
< 4 个	7 (24.14)	30 (49.18)		

表2 SHPT患者PTX术后发生SH的多因素logistic分析

Table 2 Multivariate logistic analysis of SH after PTX in SHPT patients

变量	β	Wald (χ^2)	P	OR	95%CI
术前ALP	0.028	4.937	0.013	1.442	1.334~5.881
术前ALB	0.316	5.042	0.017	1.391	1.168~3.159
甲状旁腺切除数 \geq 4个	1.473	7.038	0.002	2.248	1.211~7.352

表3 术前ALB、ALP水平对SHPT患者PTX术后发生SH的预测价值

Table 3 Predictive value of preoperative ALB and ALP levels on SH after PTX in SHPT patients

自变量	AUC	标准误	P	95%CI
术前ALP	0.729	0.070	0.006	0.586~0.872
术前ALB	0.714	0.073	0.010	0.577~0.850

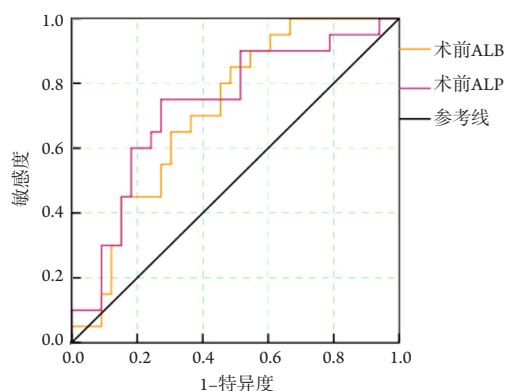


图1 术前ALP、ALB水平对SHPT患者PTX术后SH发生的预测效能

Figure 1 Predictive efficacy of preoperative ALP and ALB levels on SH after PTX in SHPT patients

3 讨论

慢性肾脏病(chronic kidney disease, CKD)是SHPT最常见病因,且随CKD分期增加,SHPT发生率也明显增加^[6]。SHPT患者体内PTH分泌异常增加和甲状旁腺代偿性增生,易对患者骨骼、皮肤、心血管和神经等全身组织系统产生不良影响。既往研究^[7]认为:SHPT已成为影响CKD患者生存质量的危险因素,其中心血管和组织钙化是CKD患者的常见死亡原因。因此对于药物治疗效果差、临床症状体征明显的SHPT患者,排除手术禁忌证后均应积极接受多学科协作手术治疗。

SH是PTX手术患者的突出并发症,发生率为30%~60%^[8-9]。若能术前预测SH的发生风险,对临

床识别SH高危人群、指导补钙治疗和提高SH防治水平有重要意义。本研究显示:SH组术前ALP水平、甲状旁腺切除数 \geq 4个者均高于对照组,术前ALB水平低于对照组;术前ALP、甲状旁腺切除个数 \geq 4个均是PTX术后SH发生的危险因素。结果与已有报道^[10]相符。对于此类危险人群术后更应密切监测血钙水平和观察症状体征表现,尽早接受补钙治疗,对促进低钙血症恢复和预防SH有益。ALP主要由肝和成骨细胞分泌,是骨基质矿化的关键酶,在排除肝脏疾病的情况下,ALP可作为评估骨营养状态的重要指标,与PTH有密切相关性,后者可调节钙磷激素平衡,具有抑制骨重建的作用^[11]。ALP水平越高,反映体内成骨细胞活跃,骨形成和骨重建的活跃性增加,因此SHPT患者多存在代谢性骨病,引起骨骼肌肉疼痛现象。SHPT患者PTX术后PTH骤然下降,对骨重建的抑制作用明显减弱,骨组织对血钙的吸收量明显增加,血钙水平明显下降,易导致SH发生。因此术前ALP水平越高,PTX术后骨饥饿状态和骨重建越明显,是SH发生的危险因素。既往研究^[12]认为术前ALP水平 \geq 600 U/L是持续性SH的独立危险因素。

ALB是人体总蛋白的主要组成部分,ALB降低多见于慢性肝炎、肝硬化和肾病综合征等肝肾疾病以及营养不良、结核病和恶性肿瘤。研究^[13]发现:入院时较低的ALB水平可作为特重度烧伤患者SH发生的独立危险因素,原因与创伤炎症反应后毛细血管通透性增加和ALB渗漏至组织间隙有关,造成血钙流失。ALB与PTX术后SH发生的关系尚不明确。本研究发现术前ALB也是PTX术后

SH发生的危险因素,提示术前ALB水平偏高者存在更高的术后SH发生风险。ROC曲线分析显示:术前ALB水平 >38.72 g/L时,预测PTX术后SH发生的AUC为0.714(95%CI: 0.577~0.850),准确性尚可,虽略低于术前ALP的AUC为0.729,但二者AUC差异并不显著。表明术前ALB对PTX术后SH发生也具有一定预测价值,与以往研究^[14-15]的结论相符。术前ALB水平对PTX术后SH的影响机制尚不明确,推测可能原因为ALB是血浆蛋白含量最高的蛋白质,对人体骨骼发育和钙吸收有促进作用。ALB同时也是血钙离子的主要载体蛋白,是调节血钙水平的重要影响因子。术前ALB水平较高者钙结合蛋白增加,钙结合蛋白进入组织间隙聚集,肠道和骨骼系统的钙吸收作用增强,但血钙水平有所下降。Donahue等^[16]指出:术前低血钙水平是PTX术后SH发生的危险因素,但此结论仍需大样本量去佐证。与术前ALB水平偏低者相比,术前ALB水平较高者PTX术后骨饥饿状态更明显^[17],骨重建过程中钙、磷沉积增加,加剧血钙水平下降,可能是低钙血症和SH发生的原因之一,但其具体影响机制仍有待深入探究。

本研究存在一些不足:为单中心回顾性研究,且样本量偏少,可能对研究结论产生一定偏倚;未能深入探讨术前ALB与PTX术后SH发生的作用机制。本研究结果表明SHPT患者术前ALB水平是PTX术后SH发生的危险因素,对初步筛选风险人群和预测SH发生有一定价值。

参考文献

- 李昱洁,余跃天,殷荣,等.继发性甲状旁腺功能亢进患者术后严重低钙血症的危险因素[J].临床与病理杂志,2019,39(7):1513-1520.
LI Yujie, YU Yuetian, YIN Rong, et al. Risk factors for post parathyroidectomy hypocalcemia in patients with secondary hyperparathyroidism[J]. Journal of Clinical and Pathological Research, 2019, 39(7): 1513-1520.
- 赵沙沙,闻萍,甘巍,等.继发性甲状旁腺功能亢进症甲状旁腺切除术后并发症分析[J].肾脏病与透析肾移植杂志,2019,28(1):25-29.
ZHAO Shasha, WEN Ping, GAN Wei, et al. Complications after parathyroidectomy for secondary hyperparathyroidism[J]. Chinese Journal of Nephrology, Dialysis & Transplantation, 2019, 28(1): 25-29.
- Lin CH, Chiu YC, Lee CS. Hypocalcemia-associated mania after parathyroidectomy[J]. Bipolar Disord, 2020, 22(7): 766-767.
- 宋岩,杨虎,林琳,等.白蛋白-胆红素评分在自身免疫性肝炎肝硬化预后评估中的应用[J].中华肝脏病杂志,2019,27(10):772-776.
SONG Yan, YANG Hu, LIN Lin, et al. Albumin-to-bilirubin scores for assessing the prognosis in autoimmune hepatitis-related cirrhosis[J]. Chinese Journal of Hepatology, 2019, 27(10): 772-776.
- Benabdelkamel H, Masood A, Ekhzaimy AA, et al. Proteomics profiling of the urine of patients with hyperthyroidism after anti-thyroid treatment[J]. Molecules, 2021, 26(7): 1991-1997.
- Galassi A, Ciceri P, Fasulo E, et al. Management of secondary hyperparathyroidism in chronic kidney disease: a focus on the elderly[J]. Drugs Aging, 2019, 36(10): 885-895.
- 李艺,丁国华.继发性甲状旁腺功能亢进症治疗现状的研究进展[J].中华实用诊断与治疗杂志,2020,34(7):753-756.
LI Yi, DING Guohua. Progress in treatment of secondary hyperparathyroidism[J]. Journal of Chinese Practical Diagnosis and Therapy, 2020, 34(7): 753-756.
- Unsal IO, Calapkulu M, Sencar ME, et al. Preoperative vitamin D levels as a predictor of transient hypocalcemia and hypoparathyroidism after parathyroidectomy[J]. Sci Rep, 2020, 10(1): 9895-9900.
- 吴丽英,刘映红.西那卡塞治疗血液透析患者继发性甲状旁腺功能亢进的临床研究[J].川北医学院学报,2018,33(1):29-32.
WU Liying, LIU Yinghong. Clinical study on cinacalcet in the treatment of secondary hyperparathyroidism in patients treated with hemodialysis[J]. Journal of North Sichuan Medical College, 2018, 33(1): 29-32.
- 张洪彬,赵寒辉,王素霞,等.303例甲状旁腺切除术围术期观察及术后严重低钙血症危险因素分析[J].山东大学学报(医学版),2020,58(9):14-20.
ZHANG Hongbin, ZHAO Hanhui, WANG Suxia, et al. Perioperative observation and postoperative risk factors of severe hypocalcemia after parathyroidectomy: a report of 303 cases[J]. Journal of Shandong University. Medical Edition, 2020, 58(9): 14-20.
- 赵耘,刘敏.低磷酸酶血症治疗新进展[J].中华实用儿科临床杂志,2021,36(2):151-154.
ZHAO Yun, LIU Min. New progress in treatment of hypophosphatasia[J]. Chinese Journal of Applied Clinical Pediatrics, 2021, 36(2): 151-154.
- Philips R, Nulty P, Seim N, et al. Predicting transient hypocalcemia in patients with unplanned parathyroidectomy after thyroidectomy[J]. Am J Otolaryngol, 2019, 40(4): 504-508.
- 吴静,张勤,刘健,等.特重度烧伤患者早期发生严重低钙血症的影响因素与临床意义[J].中华烧伤杂志,2018,34(4):203-207.
WU Jing, ZHANG Qin, LIU Jian, et al. Influencing factors and clinical significance of severe hypocalcemia in patients with extremely severe burns in early stage[J]. Chinese Journal of Burns, 2018, 34(4):

- 203-207.
14. Fonseca-Correa JI, Nava-Santana C, Tamez-Pedroza L, et al. Clinical factors associated with early and persistent hypocalcaemia after parathyroidectomy in patients on dialysis with severe hyperparathyroidism[J]. *Nephrology (Carlton)*, 2021, 26(5): 408-419.
 15. 顾恒, 耿小平, 陈江明, 等. 继发性甲状旁腺功能亢进患者术后持续性严重低钙血症的相关因素分析[J]. *中华内分泌代谢杂志*, 2018, 34(1): 57-60.
GU Heng, GENG Xiaoping, CHEN Jiangming, et al. Related factor analysis for persistent severe hypocalcemia after parathyroidectomy in secondary hyperparathyroidism patients[J]. *Chinese Journal of Endocrinology and Metabolism*, 2018, 34(1): 57-60.
 16. Donahue C, Pantel HJ, Yarlalagadda BB, et al. Does preoperative calcium and calcitriol decrease rates of post-thyroidectomy hypocalcemia? A randomized clinical trial[J]. *J Am Coll Surg*, 2021, 232(6): 848-854.
 17. Wang M, Chen B, Zou X, et al. A nomogram to predict hungry bone syndrome after parathyroidectomy in patients with secondary hyperparathyroidism[J]. *J Surg Res*, 2020, 255: 33-41.

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