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继发性甲状旁腺机能亢进患者在血透基础上联用骨化三醇后 ALP、iPTH 指标变化探究 *

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摘要 目的: 探讨继发性甲状旁腺机能亢进患者在血透基础上联用骨化三醇后全段甲状旁腺激素 (intact parathyroid hormone, iPTH)、碱性磷酸酶 (alkaline phosphatase, ALP) 指标变化情况。**方法:** 选取我院 2019 年 1 月到 2019 年 12 月共收治的维持血液性透析继发性甲旁亢患者 80 例, 随机分为两组, 每组 40 例, 给予对照组常规治疗方式, 给予观察组在血透基础上联用骨化三醇治疗, 对比两组的治疗效果、血液相关指标变化以及不良反应的发生情况。**结果:** 对照组治疗总有效率为 72.5 %, 观察组的治疗总有效率为 90.0 %, 观察组明显优于对照组 ($P < 0.05$); 两组治疗前 iPTH、ALP、磷(P)、钙(Ca)无明显差异 ($P > 0.05$), 治疗后观察组前 iPTH、ALP、P、Ca 相关血液指标明显优于对照组 ($P < 0.05$); 对比两组不良反应发现, 患者在治疗后不良反应发生率无明显差异 ($P > 0.05$)。**结论:** 对继发性甲旁亢患者在血透基础上联用骨化三醇能够提高患者的治疗效果, 改善患者相关血液指标情况, 而且不良反应发生情况与常规治疗没有明显差异, 安全可靠, 值得临床应用推广。

关键词: 继发性甲旁亢; 血液透析; 骨化三醇; 甲状旁腺亢进

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ALP and iPTH Index Levels in Patients with Secondary Hyperthyroidism Combined with Calcitriol Based on Hemodialysis*

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ABSTRACT Objective: To investigate the changes of ALP and iPTH indexes in patients with secondary hyperthyroidism combined with calcitriol on the basis of hemodialysis. **Methods:** A total of 80 patients with secondary hyperthyroidism who maintained hemodialysis who were admitted to our hospital from January 2019 to December 2019 were selected as the research object. The patients were randomly divided into an observation group and a control group. Each group of 40 patients was given The patients in the control group were given conventional treatment, and the patients in the observation group were treated with calcitriol on the basis of hemodialysis, and the treatment effects, changes in blood-related indicators, and the incidence of adverse reactions were compared between the two groups. **Results:** The total effective rate of treatment in the control group was 72.5 %, and the total effective rate in the observation group was 90.0 %. The observation group was significantly better than the control group ($P < 0.05$). The iPTH, ALP, P, Ca of the two groups of patients before treatment There was no significant difference ($P > 0.05$). After treatment, the blood parameters related to iPTH, ALP, P, and Ca in the observation group were significantly better than those in the control group ($P < 0.05$). Comparing the adverse reactions between the two groups, the incidence of adverse reactions after treatment was found in the patients There was no significant difference ($P > 0.05$). **Conclusion:** Combined use of calcitriol on the basis of hemodialysis in patients with secondary hyperthyroidism can improve the patient's treatment effect and improve the patient's related blood indicators, and the occurrence of adverse reactions is not significantly different from conventional treatment. It is safe and reliable, and is worthy of clinical Application promotion.

Key words: Secondary hyperthyroidism; Hemodialysis; Calcitriol; Hyperparathyroidism

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前言

继发性甲状旁腺功能亢进症简称继发性甲旁亢 (SHPT),

是维持性血液透析患者的常见并发症, 主要是患者的甲状旁腺分泌过量的甲状旁腺激素所导致, 早期可无症状, 除骨骼严重损害外, 还可加剧钙磷代谢异常, 引起患者皮肤瘙痒、贫血、神

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经系统和心血管系统等组织器官的损害^[1-3]。当前,临床医学中对于继发性甲状旁腺功能亢进症一般采取药物性的保守治疗,这样不仅能够保护患者的心脏功能,而且能够缓解甲旁亢的相关症状^[4,5]。临床上常用的治疗药物有阿法骨化醇和骨化三醇,骨化三醇属于一种活性比较强的 1,25-二羟代谢物^[6],能够直接作用于甲状旁腺,减少甲状旁腺组织的增生,抑制 PTH 的合成和分泌^[7,8]。本文选取我院 2019 年 1 月到 2019 年 12 月共收治的维持血液性透析继发性甲旁亢患者 80 例,分析继发性甲旁亢患者在血透基础上联用骨化三醇后 ALP、iPTH 指标变化。

1 资料与方法

1.1 一般资料

选取我院 2019 年 1 月到 2019 年 12 月共收治的维持血液性透析继发性甲旁亢患者 80 例,随机分为两组,每组 40 例。所有患者血液透析治疗时间均超过三年,且伴随继发性甲旁亢症状^[9];患者均曾经接受过传统的活性维生素 D 和钙剂治疗,但是 iPTH 水平一直持续不下;患者均患有中度或重度继发性甲旁亢,血液中 iPTH 高于 400 pg/L^[10]。两组的一般资料对比无差异($P>0.05$),有可比性,如表 1。

表 1 两组一般资料对比

Table 1 Comparison of general information between the two groups

Groups	n	Gender (Male/female)	Age (years)	Course of disease (years)	Primary disease				
					Diabetic nephropathy	Lupus nephritis	Chronic glomerulitis	Hepatitis B related nephritis	Other
Observation group	40	21/19	62.6± 7.5	1.6± 0.3	15	8	7	6	4
Control group	40	22/18	63.3± 8.2	1.5± 0.4	14	9	6	4	7

1.2 方法

两组均采用金宝 AK96 透析机,使用旭化成聚砜膜透析器,透析液:碳酸氢盐透析液,血流量 280 mL/min,透析液流量 500 mL/min,透析时间 4 h/次,3 次/w。均给予以下药物进行常规治疗:左卡尼汀(广州白云山明兴制药有限公司;国药准字:H20123426)1 g 皮下注射,2 次/w,促红细胞生成素 4000~10000 U 皮下注射,1 次/w,苯磺酸氨氯地平 5 μg 口服,2 次/w,同时给予低磷及低蛋白饮食。对照组患者在此基础上,口服阿仑膦酸钠片(Merck Sharp&Dohme Italia SPA; 国药准字 J20130085),每次 10 mg,一日两次。观察组患者在基础甲旁亢药物治疗基础上口服骨化三醇(正大制药(青岛)有限公司;国药准字:H20030491),每天 0.25 μg。两组患者的治疗时间均为 8 w。

1.3 观察指标

观察指标:观察两组治疗前后 iPTH、ALP、P、Ca 的水平情况;观察两组头痛、口腔金属味、局部疼痛、血管性水肿以及恶

心呕吐等不良反应发生情况。

疗效判断,疗效判定标准^[11,12]:显效,甲状旁腺激素下降超过 75%;有效,甲状旁腺激素下降 25%~75%;无效,甲状旁腺激素下降不超过 25%,总有效率=显效率+有效率。

1.4 统计学方法

采用 SPSS 20,以($\bar{x} \pm s$)表示 iPTH、ALP、P、Ca 数值等计量资料,采取 t 检验;以 n(%)表示计数资料,采取 χ^2 检验。 $P<0.05$ 有统计学意义。

2 结果

2.1 疗效对比

对照组治疗总有效率为 72.5%,观察组的治疗总有效率为 90.0%,观察组明显优于对照组($\chi^2=0.045$, $P<0.05$),如表 2 所示。

表 2 两组疗效比较(例,%)

Table 2 Comparison of clinical effect between two groups (n,%)

Groups	n	Marked effect	Effective	Invalid	Total efficiency
Observation group	40	12(30.0)	24(60.0)	4(10.0)	36(90.0)*
Control group	40	11(27.5)	18(45.0)	11(27.5)	29(72.5)

Note: Compared with the control group, * $P<0.05$.

2.2 两组血液相关指标变化分析

两组继发性甲旁亢患者在用药治疗之前 iPTH、ALP、P、Ca 指标对比无明显差异($P>0.05$),通过 8 w 时间的治疗之后,观察组的 iPTH、ALP、P 指标明显低于对照组,Ca 明显高于对照组($P<0.05$),如表 3 所示。

2.3 两组不良反应发生情况比较

对比两组不良反应发现,患者在治疗后不良反应发生率无明显差异($P>0.05$),如表 4 所示。

3 讨论

据统计数据表明^[13,14],我国当前慢性肾脏疾病的患病率高达 10%。慢性肾功能衰竭维持血液透析的患者多伴有皮肤瘙痒、关节痛、神经损害等,分析其机制主要与钙磷代谢紊乱、甲状旁腺功能亢进相关^[15,16]。血液透析治疗为当前慢性肾脏疾病的主要方法,可改善慢患者的生活质量,从而提升长期生存率^[17,18]。然而随着患者透析时间的不断增长,虽然应用血液透析

表 3 两组血液相关指标变化分析($\bar{x} \pm s$)Table 3 Analysis of changes in blood-related indexes in two groups ($\bar{x} \pm s$)

Groups	n	iPTH(pg,L)		ALP(U,L)		P(mmol,L)		Ca(mmol,L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	40	420.19±52.02	210.03±21.54* [#]	159.53±28.21	72.59±8.52* [#]	1.93±0.08	1.33±0.06* [#]	1.99±0.14	2.13±0.27* [#]
Control group	40	422.21±53.06	318.23±35.68*	160.58±28.15	127.62±10.78*	1.94±0.07	1.64±0.08*	1.97±0.12	2.61±0.46*

Note: Compared with the control group, * $P<0.05$; compared with before treatment, [#] $P<0.05$.

表 4 两组不良反应发生情况(例,%)

Table 4 The occurrence of adverse reactions in two groups of patients (n,%)

Groups	n	Headache	Oral metallic taste	Local pain	Angioedema	Feel sick and vomit	Total incidence
Control group	40	2(5.0)	1(15.63)	2(5.0)	2(5.0)	1(2.5)	8(20.0)
Observation group	40	1(2.5)	1(2.5)	1(2.5)	2(5.0)	1(2.5)	6(15.0)

治疗患者的生存时间和生存率明显提升,但是治疗过程中伴随的并发症也逐渐增多,残余肾功能减低,钙磷代谢问题日渐显著^[19,20]。为了减少患者相关并发症的发生,对于血液透析患者,稳定钙磷、甲状旁腺激素、骨异常是主要目标^[21]。由于人类肾脏是合成 1,25(OH)₂D₃ 的重要器官,一旦患者出现慢性肾功能衰竭时,1,25(OH)₂D₃ 的合成会逐渐减少,这也是患者在血液透析之后容易引发继发性甲旁亢的一个关键性因素^[22,23]。iPTH 是由甲状旁腺分泌的物质,它对于人体的不同气管都能够起到靶向作用,iPTH 出现异常对多个器官造成影响^[24]。iPTH 和 1,25(OH)₂D₃ 之间关系非常密切,主要是因为 1,25(OH)₂D₃ 可以直接对甲状旁腺的细胞增生产生抑制,从而对于 1,25(OH)₂D₃ 的抵抗功能也有所下降,从而抑制 iPTH 的合成和分泌,并且血钙对于甲状旁腺抑制的敏感性也增强^[25,26]。

骨化三醇应用后在体内不受肝肾经化作用就可发挥其作用,增加甲状旁腺细胞维生素 D 受体的表达^[27,28],反馈性的抑制 iPTH 合成,增加对甲状旁腺对钙的敏感性,起到降低 iPTH 及调节血钙的作用。此外,骨化三醇可被小肠快速吸收,无需代谢活化,起效快、毒副作用小。

本研究结果显示,对照组患者治疗总有效率为 72.5%,观察组患者的治疗总有效率为 90.0%,观察组明显优于对照组,与韩鸚羸^[29]等学者的研究一致,该学者探究骨化三醇联合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疗效,结果显示治疗组的总有效率为 94.0%,显著高于对照组的 82.0%;同时国外学者 Carroll B^[30]研究也显示,骨化三醇能降低 iPTH 及调节血钙的作用,从而提升患者的治疗效果。本研究结果显示,继发性甲旁亢患者在血透基础上联用骨化三醇治疗效果更好。两组患者治疗前 iPTH、ALP、P、Ca 无明显差异,治疗后观察组前 iPTH、ALP、P、Ca 相关血液指标明显优于对照组,与王辉^[31]等学者的研究类似,该学者探讨骨化三醇联合西那卡塞治疗维持性血液透析患者继发性甲状旁腺功能亢进的疗效和安全性,结果显示与治疗前比较,治疗 1、3、6 个月时,患者血清 iPTH、P 均明显降低,Ca 均明显升高;费良玉^[32]等的研究也显示,西那卡

塞联合骨化三醇治疗维持性血液透析患者伴难治性继发性甲状旁腺功能亢进,西那卡塞联合小剂量骨化三醇治疗后,P、iPTH、ALP 均较治疗前下降,但是 Ca 与本研究不同,也是降低的,可能与研究对象的患者的基础患病有关,说明 Ca 不是检测的特异性指标。但是后续也需要进一步的研究,分析影响 Ca 变化的因素。由此证明,两组治疗方案均能降低 iPTH 的水平,虽然血钙升高,但在正常值范围内,提示骨化三醇对促进 iPTH 下降效果更好。两组在治疗后不良反应发生率无明显差异,表明在常规继发性甲旁亢治疗的基础上加用骨化三醇不会增加患者的不良反应,安全性好。本结果与 De Graeff^[33]学者研究一致^[33],其结果中骨化三醇治疗血透基础上继发性甲旁亢患者 iPTH、ALP、P、Ca 指标差异显著,研究具有作证意义。同时王辉^[31]的研究也发现治疗过程中出现恶心呕吐 4 例,腹痛 2 例,肌痛 1 例,经内科对症治疗后缓解。因此说明骨化三醇联合血透治疗继发性甲旁亢,安全性好。本研究也存在一定的不足,没有设立单独应用骨化三醇治疗继发性甲旁亢,同时纳入的研究对象少,后续研究需要扩大样本量进行深入探究治疗的机制。

总而言之,对继发性甲旁亢患者在血透基础上联用骨化三醇治疗效果显著,能够改善患者 iPTH、ALP、P、Ca 的水平,安全性好,值得临床推广应用。

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