

· 临床研究 ·

甲状旁腺切除加自体移植术对尿毒症患者近期临床症状及钙磷代谢的影响(附 20 例临床分析)

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中图分类号: R582.1 文献标识码: A 文章编号: 1006-7108(2016) 10-1288-05

摘要: 目的 观察甲状旁腺切除加自体移植(parathyroidectomy with autotransplantation, PTX + AT)对尿毒症继发性甲状旁腺功能亢进症(secondary hyperparathyroidism, SHPT)患者近期临床症状及各项生化指标的影响。方法 回顾性分析 20 例 SHPT 手术前和手术后短期内的临床症状、血清全段甲状旁腺激素(intact parathyroid hormone, iPTH)、血钙、血磷等变化以及术后近期疗效及并发症的发生情况。结果 20 例尿毒症继发性甲状旁腺功能亢进症患者,术前 iPTH 为(1648 ± 797) pg/mL,甲状旁腺切除后,术后 1w iPTH 为(125 ± 263) pg/mL, $P < 0.01$, 差异具有统计学意义。术前血钙(2.58 ± 0.25) mmol/L、血磷(2.30 ± 0.73) mmol/L;术后第 1 天血钙(1.97 ± 0.46) mmol/L、血磷(1.92 ± 0.81) mmol/L,术后 1w 血钙(1.99 ± 0.46) mmol/L、血磷(1.38 ± 0.66) mmol/L。术后 1w 15 例患者(占总失眠人数 100%)失眠症状,13 例患者(占总皮肤瘙痒人数 80%)皮肤瘙痒症状、3 例患者(占不安腿人数 100%)不安腿症状明显好转,12 例患者(占骨关节痛患者 80%)骨关节疼痛症状、5 例患者(占肌无力患者 60%)肌无力症状有所改善。术后 5 位患者出现抽搐,4 例患者出现声音嘶哑,经相应处理后,患者症状明显改善。**结论** 甲状旁腺切除在短期内显著改善尿毒症继发性甲状旁腺功能亢进患者的骨关节痛、皮肤瘙痒、肌无力、失眠等临床症状,同时缓解高钙、高磷血症。

关键词: 尿毒症;甲状旁腺功能亢进;甲状旁腺切除;钙磷代谢

Effects of parathyroidectomy and autotransplantation on short-term clinical symptoms and calcium phosphorus metabolism in uremic patients

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Abstract: Objective To study the effect of parathyroidectomy with autotransplantation (PTX + AT) on short-term physiological indicators in patients with uremic secondary hyperparathyroidism (SHPT). **Methods** Retrospective analysis was made on the short-term clinical symptoms of 20 patients with uremic SHPT who underwent PTX + AT, including the changes of their serum calcium (Ca), phosphorus (P) and intact parathyroid hormone (iPTH) before and after the operations, as well as their postoperative curative effect and complications. **Result** In all 20 uremic SHPT, the mean iPTH was (1648 ± 797) pg/mL before operation and was (125 ± 263) pg/mL on the 7th day after operation, the difference is statistically significant ($P < 0.01$). The mean serum calcium and phosphorus before operation were (2.58 ± 0.25) and (2.30 ± 0.73) mmol/L, respectively. On the first day after the operation, the mean serum calcium and phosphorus were (1.97 ± 0.46) mmol/L and (1.92 ± 0.81) mmol/L, respectively, while the means at a week after were (1.99 ± 0.46) mmol/L and (1.38 ± 0.66) mmol/L, respectively. One week after the operation, 15 patients with insomnia (accounting for 100% of total number of patients with insomnia), 13 cases with itchy skin (accounting for 80% of patients with itchy skin) and 3 patients with symptoms of restless legs symptoms (accounting for 100% of patients with restless legs symptoms) improved markedly. Besides, 12 patients with symptoms of joint pain (accounting for 80% of patients with joint pain) and 5 patients with symptoms of muscle weakness (accounting for 60% of patients with muscle

基金项目: 安徽省自然科学基金项目(1308085MH155)

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weakness) also improved. Five patients experienced convulsions and four patients suffered hoarseness after the operation. However, after appropriate treatment, the symptoms improved significantly. **Conclusion** Removal of Parathyroid gland can, in a short time, significantly relieve joint pain, itching, muscle weakness, insomnia and other symptoms of the uremia patients with secondary hyperparathyroidism. It can also alleviate high calcium and hyperphosphatemia.

Key words: Uremia hyperparathyroidism; Parathyroidectomy; Calcium phosphorus metabolism

继发性甲状旁腺功能亢进是慢性肾功能衰竭维持性透析患者的常见并发症。严重甲状旁腺功能亢进的患者药物治疗常无明显效果,且患者多有骨关节痛、肌无力、皮肤瘙痒、骨畸形、失眠等临床症状,严重影响患者的生存质量。目前采用甲状旁腺切除术加自体移植手术是治疗这一并发症的有效方法^[1]。我院肾内科近几年陆续与外科医师合作,为尿毒症并发重度甲状旁腺功能亢进的患者实施甲状旁腺切除加自体移植术,并完成术前术后患者的管理。近期疗效满意。

1 材料和方法

1.1 一般资料

20 例尿毒症继发重度甲状旁腺功能亢进症的患者,均长期维持性透析治疗,18 例来自于本院,2 例来自于外院。其中男性 10 例,女性 10 例;年龄 15 ~ 60 岁,平均(44 ± 12)岁;行血液透析 8 例,腹膜透析 12 例,透析时间 2 ~ 18 年,平均(78 ± 50)月;20 例患者原发病为慢性肾小球肾炎 19 例,狼疮肾炎 1 例。其中 15 例患者在近一年内手术(见表 1)。

1.2 术前内科处理

影像学检查:行甲状旁腺超声检查和甲状旁腺核素扫描(⁹⁹Tc^m-MIBI)进行甲状旁腺定位、心电图和超声心动图评估心血管疾病风险以及双手正位片、胸部正位片等;实验室检查:血清全段甲状旁腺激素血钙(iPTH)、血电解质、骨特异性碱性磷酸酶(ALP)、血常规、肝肾功能、止凝血等检查。术前 1 w 开始口服活性维生素 D 0.25 ~ 0.5 μg/d;术前 1 d 充分血液透析(无肝素)一次或腹膜透析。

1.3 甲状旁腺切除情况

20 例 SPTH 患者中 18 例行双侧甲状旁腺全切除加前臂或胸锁乳突肌自体移植术,2 例行甲状旁腺次全切术(其中 1 例行甲状旁腺次全切,另 1 例切除甲状旁腺 2.5 枚、保留左下半枚),切除组织送术中送快速病理提示均证实为甲状旁腺组织,术后石蜡切片病理及免疫组化显示甲状旁腺增生性病变,部分合并甲状旁腺腺瘤样结节增生。

表 1 患者一般情况及临床特征
Table 1 Patients general condition and clinical features

病例数 (case number)	20 例
男/女 (Sex)	10/10
年龄 (Age)	(44 ± 12) 岁
透析时间 (Dialysis time)	(78 ± 50) 月
血液透析/腹膜透析 (HD/PD)	8/12
骨关节痛 (Joint pain)	12
肌无力 (Muscle weakness)	5
皮肤瘙痒 (Itchy skin)	11
失眠 (Insomnia)	15
不安腿 (Restless legs)	3
骨畸形 (Bone malformation)	5
心瓣膜钙化 (Heart valve calcification)	8
骨质疏松或骨质改变 (Osteoporosis)	15
放射片提示骨异常 (Abnormal bone)	5
心脏增大 (Big heart)	10
高血压 (Hypertension)	16

1.4 术后内科处理

患者术后第三天手术切口无异常转入肾内科,常规检测患者生命体征,观察切口引流和有无呼吸困难等情况。特别注意观察有无抽搐等低钙症状。术后第 1 ~ 3 天,每日检测血清钙、磷 2 ~ 3 次,术后第 4 ~ 7 天,酌情每日检测血清钙、磷 1 ~ 2 次直至稳定。间断测定血清 PTH,碱性磷酸酶。术后常规补钙,口服和/或静滴(酌情口服碳酸钙达到元素钙 1 ~ 2 g/d,骨化三醇 1 ~ 4 μg/d)。如果血钙 < 1.8 mmol/L 或出现抽搐,立即给予 1 g 葡萄糖酸钙(即 10% 葡萄糖碳酸钙 10 mL,含钙 90 mg)静脉推注,并

以 1 g/h 葡萄糖酸钙的速度微量静脉注射泵维持。血钙恢复正常且稳定后,钙注射剂应逐渐减少,口服碳酸钙 1~2 g/d,同时予骨化三醇,每日 0.5~2 μg/d 维持。

1.5 指标观察及疗效判定

设计术前术后观察表、记录患者生化指标及患者主观感觉变化。对比患者术前、术后第 1、3 天及术后 1 w 血清钙、磷和 iPTH 水平;比较患者术前术后患者骨关节痛、肌无力、皮肤瘙痒、失眠/不安腿等临床症状的改变情况。

1.6 统计学处理

采用 SPSS 16.0 进行统计分析,定量资料采用均数±标准差表示;统计方法采用配对 *t* 检验,以 *P* < 0.05,差异有统计学意义。

2 结果

2.1 术后实验室检查

20 例患者术前 iPTH 均值为 (1648 ± 797) pg/mL,术后 1 w 患者 iPTH 值即下降明显,均值为 (125 ± 263) pg/mL,差异具有统计学意义 (*P* < 0.01),其中术后第 1 天 20 例患者中有 10 位患者 iPTH 低于 150 pg/mL,术后 1 w 有 16 位患者 iPTH 低于 150 pg/mL,有 4 例 iPTH 值虽偏高,但均明显低于术前 2~5 倍。血清钙、磷术后均下降,术后第 1 天血钙 (1.97 ± 0.46) mmol/L、血磷 (1.92 ± 0.81) mmol/L,术后第 7 天血钙 (1.99 ± 0.51) mmol/L、血磷 (1.38 ± 0.66) mmol/L。其中,血清钙下降 (*P* < 0.01),差异具有统计学意义(见表 2)。

表 2 iPTH、钙、磷浓度在手术前后的变化(*n* = 20)
Table 2 Changes in serum iPTH, calcium and phosphorus from preoperation to postoperation(*n* = 20)

项目	术前	术后 1 天	术后 3 天	术后 7 天
iPTH (pg/mL)	1648 ± 797 (<i>n</i> = 20)	290 ± 319 * (<i>n</i> = 20)	105 ± 237 (<i>n</i> = 18)	125 ± 263 * (<i>n</i> = 20)
Ca (mmol/L)	2.58 ± 0.25 (<i>n</i> = 20)	1.97 ± 0.52 * (<i>n</i> = 20)	1.91 ± 0.43 (<i>n</i> = 20)	1.99 ± 0.46 * (<i>n</i> = 20)
P (mmol/L)	2.30 ± 0.73 (<i>n</i> = 20)	1.92 ± 0.81 (<i>n</i> = 18)	1.69 ± 0.74 (<i>n</i> = 19)	1.38 ± 0.66 (<i>n</i> = 19)

注:术后与术前比较,**P* < 0.05

2.2 临床症状

20 例患者术后 1w 内皮肤瘙痒、失眠/不安腿有明显缓解。骨关节痛、肌无力有所好转(见表 3)。其中 15 例患者失眠症状、3 例患者不安腿症状及 13

例患者皮肤瘙痒症状明显好转,12 例患者骨关节疼痛症状、5 例患者肌无力症状较前有所好转,仅有少数患者症状虽然仍存在,但已经明显较术前改善(见表 3)。

表 3 患者临床症状及术后并发症在手术前后不同时间的变化情况
Table 3 Clinical symptoms and complications before and after the operation

时间 Time	术前 (Preoperation)	术后 (Postoperation)		
		第一天 (1 st day)	第三天 (3 rd day)	第七天 (7 th day)
骨关节痛 Joint pain	15	6	5	3
肌无力 Muscle weakness	8	4	3	3
皮肤瘙痒 Itchy skin	16	9	5	3
失眠 Insomnia	15	3	1	0
不安腿综合征 Restless legs	3	1	0	0
骨畸形 Bone malformation	14	14	14	14
术后 iPTH < 150 pg/mL	-	50% (10/20)	75% (15/20)	80% (16/20)
低钙血症 Hypocalcemia	-	70% (14/20)	70% (14/20)	65% (13/20)
术后抽搐 Convulsions	-	5	2	1
术后声嘶 Hoarseness	-	4	3	2

2.3 术后主要不良反应

术后第 1~3 天,5 例患者出现不同程度的抽搐症状。其中 4 例表现为面部发麻和小抽搐,仅 1 例发生四肢大抽搐。立即给予 1g 葡萄糖酸钙静脉推注,并以 1g/h 葡萄糖酸钙的速度微量静脉注射泵维持。每日检测血钙并调整补钙剂量。术后第 5~10 天所有患者症状基本消失,监测血清钙,恢复正常且稳定后改为口服钙剂。术后第一天有 4 例患者出现声音轻度嘶哑,术后第 7 天,2 例患者症状消失,另外 2 例患者症状也明显好转。

3 讨论

在慢性肾脏病晚期患者中,钙磷代谢紊乱普遍存在。一方面由于肾脏排磷减少导致磷酸盐潴留,高磷酸盐血症引起血钙降低,同时肾 1 α 羟化酶缺乏造成肠钙吸收不足导致低钙血症;另一方面由于慢性肾功能衰竭患者的肾脏不能有效降解 PTH,体内常常持续存在高水平甲状旁腺激素,使得人体骨骼处于高转运状态,骨密度降低;其余包括人体活性维生素 D 缺乏、甲状旁腺上维生素 D 受体下调、钙敏感受体下调等多种因素,在慢性肾脏病患者体内相互作用,最终导致人体矿物质代谢紊乱的出现。在早期慢性肾脏病患者中若不加以纠正会加速慢性肾脏疾病的进展^[2,3],而晚期患者中则使骨痛、严重骨质疏松、自发性骨折、纤维囊性骨炎的发生率增加。严重者出现广泛骨畸形,甚至出现退缩人综合症。同时也增加心血管负担、继发甲状旁腺功能亢进、心脏瓣膜、血管和软组织的转移性钙化等发生,增加了 CKD 患者的死亡率及主要心血管事件的发生率^[4,5],严重降低患者的生活质量。

对于慢性肾功能不全继发性甲状旁腺功能亢进,应采取分级治疗。大多数患者早期使用钙剂和活性维生素 D 联合治疗是有效的。但少数患者未及时治疗或疗效不好,甲状旁腺最终会形成功能自主的腺瘤,形成难治性甲状旁腺功能亢进症。此时内科药物治疗无明显效果,如果继续补充维生素 D 及钙剂,会使钙磷乘积增加,加速异位钙化。其中以肾性骨病、心血管系统损害,肌无力、皮肤瘙痒表现突出。严重影响患者生活质量及生存率。目前,甲状旁腺切除术是治疗尿毒症继发难治性甲旁亢的一种有效的治疗手段^[6,7],是药物治疗失败的补救措施。虽然目前一些新药如钙敏感性受体激动剂(calcimimetics)能够降低患者 iPTH 水平,但现有的研究调查显示手术切除不仅有费用低的优势,在疗

效上也优于钙敏感受体激动剂^[8,9]。

甲状旁腺全切术+自体移植主要适用于药物治疗过程中出现的顽固性高钙血症和(或)高磷血症及其引起的严重并发症患者不能耐受者,或严重甲状旁腺功能亢进^[10],血清 iPTH 明显升高及 B 超等影像学证实甲状旁腺明显增生,或一些经药物治疗仍不能控制的有严重进展症状的纤维性骨炎。

目前继发性甲状旁腺亢进的手术方法主要有 3 种^[11]:甲状旁腺次全切术、甲状旁腺全部切除+自体移植、甲状旁腺全切除但不移植。前两种手术方式均有再复发可能,第一种手术方式复发率最高,第三种手术方式可能出现难治性骨软化病,故根据目前多数临床研究,甲状旁腺切除+自体移植可以有效治疗继发性甲旁亢^[12],同时能防止甲状旁腺全切导致的难治性低钙血症的出现,能显著降低 iPTH 水平,改善患者皮肤瘙痒^[13,14]、骨痛等一些并发症症状,提高患者生活质量及营养状态^[15],若手术后复发,使再次手术切除甲状旁腺变得简单易行。

本研究通过回顾性分析这 20 例尿毒症继发重度甲旁亢患者,甲状旁腺全切+自体移植术治疗后,术后 1w 左右各项指标都较术前有较大改善。术后 1w 80% 的病例 PTH 低于 150pg/mL。临床症状尤其是皮肤瘙痒、骨痛、失眠、不安腿等症状缓解明显,且根据患者的随访效果看,生活质量明显改善。术后虽有一半以上患者发生低钙血症,但发生低钙抽搐仅 5 例,且经过积极处理后抽搐症状很快能够得到改善。我们将继续积累病例并随访观察这些患者的长期疗效及复发情况。

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(收稿日期:2016-02-28,修回日期:2016-04-13)

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室外运动,改变不健康的生活方式,适当保持体重对减少骨质疏松的发病就变得非常重要。

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(收稿日期:2016-05-15,修回日期:2016-06-22)