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重组人生长激素治疗儿童特发性矮小症的疗效及对血清 Ghrelin 和 IGF-1 水平的影响 *

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摘要 目的：探讨重组人生长激素（rhGH）治疗儿童特发性矮小症（ISS）的疗效及对血清饥饿激素（Ghrelin）、胰岛素样生长因子 -1（IGF-1）水平的影响。**方法**：选取 2014 年 1 月 -2016 年 8 月期间我院收治的 ISS 患儿 114 例为研究对象。按照随机数字表法分为实验组（n=57）与对照组（n=57）。其中对照组给予常规治疗，实验组在对照组基础上联合 rhGH 治疗，两组疗程均为 12 个月。比较两组患儿的临床疗效，同时观察并对比两组患儿治疗前后血清 Ghrelin 以及 IGF-1 水平。**结果**：治疗后两组患儿身高、生长速率均较治疗前升高，且实验组高于对照组，差异有统计学意义（*P<0.05*）；治疗后两组患儿体重、总甲状腺素、骨龄、空腹血糖水平较治疗前比较差异无统计学意义（*P>0.05*）。治疗后两组患儿血清 Ghrelin 水平较治疗前降低，且实验组低于对照组，血清 IGF-1 水平较治疗前升高，且实验组高于对照组，差异均有统计学意义（*P<0.05*）。实验组不良反应发生率为 5.26%，与对照组的 0.00%比较，差异无统计学意义（*P>0.05*）。**结论**：ISS 患儿应用 rhGH 治疗效果满意，可明显改善 ISS 患儿体内血清 IGF-1、Ghrelin 水平，安全无副作用，促进患儿健康成长。

关键词：重组人生长激素；特发性矮小症；疗效；饥饿激素；胰岛素样生长因子 -1

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Clinical Effect of Recombinant Human Growth Hormone in the Treatment of Children with Idiopathic Short Stature and its Effect on Serum Ghrelin and IGF-1 Levels*

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ABSTRACT Objective: To investigate the clinical effect of recombinant human growth hormone (rhGH) in the treatment of children with idiopathic short stature (ISS) and the effects of serum Ghrelin (Ghrelin), insulin-like growth factor -1 (IGF-1) levels. **Methods:** 114 children with ISS who were treated in our hospital from January 2014 to October 2016 were selected as the research objects. The patients were divided into two groups according to the random number table: the experimental group (n=57) and the control group (n=57). The control group was given conventional treatment, and the experimental group was treated with rhGH on the basis of the control group. The clinical efficacy of the two groups after treatment was compared, the levels of serum Ghrelin and IGF-1 were observed and compared between the two groups before and after treatment. **Results:** The height and growth rate of the two groups after treatment were higher than before treatment, and the experimental group was higher than that of the control group, the differences were statistically significant (*P<0.05*). There were no significant differences in weight, total thyroxine, bone age and fasting blood glucose level between the two groups after treatment (*P>0.05*). The level of Ghrelin in two groups after treatment was lower than that before treatment, and the experimental group was lower than that of the control group, the level of IGF-1 in two groups after treatment was higher than before treatment, and the experimental group was higher than that of the control group, the differences were statistically significant (*P<0.05*). The incidence of adverse reactions in the experimental group was 5.26%, while that of the control group was 0.00%, there was no significant difference in the incidence of adverse reactions between the two groups (*P>0.05*). **Conclusion:** The treatment of rhGH in children with ISS is satisfactory, can significantly improve the serum IGF-1 and Ghrelin levels in children with ISS, safety and no side effects, and promote the healthy growth of children.

Key words: Recombinant human growth hormone; Idiopathic short stature; Clinical effect; Ghrelin; Insulin-like growth factor -1

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前言

特发性矮小症(idiopathic short stature,ISS)是指生长激素水平正常,但发病机制尚不十分明确的身材矮小现象,是儿童时期身材矮小的常见病因[1,2]。目前为止,我国儿童 ISS 发病率约为 3%,且发病率呈逐年上升的趋势[3]。与正常儿童相比,虽然 ISS 患儿智商处于正常范围,但大多数患儿均存在内向、情绪不稳、社交退缩等心理障碍,给患儿未来生活造成重大影响[4,5]。目前临床对于该病的主要治疗方式为营养支持、运动治疗、药物治疗等,其中药物治疗效果最佳[6,7]。重组人生长激素(recombinant human growth hormone,rhGH) 是目前临床上常用的治疗 ISS 药物[8,9],rhGH 虽逐渐被临床接受,但关于其治疗 ISS 的疗效仍存在争议,认为其有效、无效的报道屡见不鲜,对最终的成年身高有无影响尚存在争议。相关报道认为,血清胰岛素样生长因子 -1(insulin-like growth factors,IGF-1)可作为判断和预测治疗 ISS 患儿的临床疗效指标之一 [10]。另有学者指出,ISS 患儿血清饥饿激素(Ghrelin)水平异常升高[11]。因此,本研究通过观察本院收治的 ISS 患儿的临床疗效以及血清 Ghrelin、IGF-1 的水平变化,旨在探讨 rhGH 对 ISS 患儿的影响,现整理报道如下。

1 资料和方法

1.1 一般资料

选取 2014 年 1 月 -2016 年 8 月期间我院收治的 ISS 患儿 114 例为研究对象。纳入标准[12]:(1)所有患儿均符合 ISS 的相关诊断标准, 并经影像学或者实验室检查等确诊,ISS 诊断标准:出生时体质量无异常,儿童时期身高低于同年龄、同性别的正常身高平均值两个 SD,骨龄落后至少 2 年,每年生长速率约小于 5 cm 则认为生长速度减慢 (采用中国人骨成熟评价标准(CHN)进行);(2)饮食、心理等无异常者;(3)染色体检查正常者;(4)患儿家属知情本研究并签署知情同意书。排除标准:(1)血常规、肝肾功能异常者;(2)合并先天性疾病者;(3)营养不良,甲状腺功能低下者;(4)对本次研究使用药物过敏者;(5)合并特纳综合征者;(6)入院前接受过其他药物治疗者;(7)临床资料不完整者。按照随机数字表法分为实验组(n=57)与对照组(n=57)。其中实验组男 32 例, 女 25 例, 年龄 7-13 岁, 平均(10.21± 1.38)岁;身高 82-141 cm,平均(109.18± 7.65)cm;骨龄 5-11 岁,平均(8.93± 1.09)岁。对照组男 30 例,女 27 例,年龄 8-14 岁, 平均 (10.35± 1.56) 岁; 身高 83-140 cm, 平均(108.48± 8.32)cm;骨龄 6-12 岁,平均(9.02± 1.26)岁。两组患儿一般资料对比差异无统计学意义(*P>0.05*),可行组间比较。本研究经医院伦理委员会批准同意。

1.2 方法

1.2.1 治疗方法 对照组患儿给予常规营养治疗, 包括饮食合理,加强补充钙质、微量元素、维生素等。实验组在对照组的基础上给予注射用 rhGH(长春金赛药业有限责任公司,国药准字:S20050025,30 IU/10 mg/3 mL/ 瓶)0.15 IU/kg 治疗,1 次/d,于睡前 0.5 h 经皮下注射。两组患儿疗程均为 12 个月。治疗前、治疗后分别由专业医师对两组患儿进行身高、体重等测量,同一时间段连测 3 次,取平均值。并于治疗前后拍 X 线片检测骨龄。

1.2.2 血清指标 所有患儿均于治疗前后抽取清晨空腹静脉血 6 mL,2800 r/min 离心 8 min,离心半径 6 cm,取上清液,置于 -30℃温箱中待测。采用酶联免疫吸附法检测血清 Ghrelin 水平,试剂盒购自上海江莱生物科技有限公司。采用全自动免疫化学发光法测定血清 IGF-1 水平,试剂盒由本院特检中心化验室提供,严格按照试剂盒说明书进行操作。空腹血糖水平采用全自动生化分析仪进行检测。采用酶联免疫吸附法检测总甲状腺素水平,试剂盒由本院特检中心化验室提供。

1.3 观察指标

检测并记录所有患儿治疗前后的身高、体重、总甲状腺素、骨龄、生长速率、空腹血糖水平等,并行组间比较,同时观察并对比两组患儿治疗前后血清 Ghrelin 以及 IGF-1 水平, 观察两组用药后不良反应情况。

1.4 统计学方法

采用 SPSS21.0 统计学软件对数据进行处理, 计数资料以率的形式表示,采用 x^2 检验,计量资料以($\bar{x}\pm s$)的形式表示,采用 t 检验,检验标准设置为 α=0.05。

2 结果

2.1 两组患儿治疗前后临床疗效比较

治疗前两组患儿身高、体重、总甲状腺素、骨龄、生长速率、空腹血糖水平等比较差异无统计学意义(*P>0.05*);治疗后两组患儿身高、生长速率均较治疗前升高,且实验组高于对照组,差异有统计学意义(*P<0.05*);治疗后两组患儿体重、总甲状腺素、骨龄、空腹血糖水平较治疗前比较差异无统计学意义 (*P>0.05*)。详见表 1。

表 1 两组患儿治疗前后临床疗效比较($\bar{x}\pm s$)

Table 1 Comparison of clinical efficacy between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Time	Height(cm)	Weight(kg)	Total thyroxine (mmol/L)	Bone age(years old)	Growth rate (cm/year)	Fasting blood glucose(mmol/L)
Control group	57	Before treatment	108.48± 8.32	33.35± 8.04	102.18± 8.55	9.02± 1.26	4.21± 0.25	4.56± 0.48
		After treatment	113.30± 7.95	34.09± 9.52	104.01± 9.04	10.31± 1.79	7.93± 3.09	4.71± 0.37
Experimental group	57	Before treatment	109.18± 7.65	33.61± 7.86	101.98± 9.13	8.93± 1.09	4.09± 0.35	4.61± 0.55
		After treatment	120.90± 10.42*	35.11± 9.62	103.85± 10.12	10.56± 1.72	9.23± 3.43*	4.68± 0.42

2.2 两组患儿治疗前后血清 Ghrelin、IGF-1 水平比较

治疗前两组患儿血清 Ghrelin、IGF-1 水平比较差异无统计学意义（*P>0.05*）；治疗后两组患儿血清 Ghrelin 水平较治疗前降低，且实验组低于对照组，血清 IGF-1 水平较治疗前升高，且实验组高于对照组，差异均有统计学意义（*P<0.05*）。详见表 2。

表 2 两组治疗前后血清 Ghrelin、IGF-1 水平比较（$\bar{x}\pm s$）

Table 2 Comparison of serum Ghrelin and IGF-1 levels between the two groups before and after treatment ($\bar{x}\pm s$)

Groups	n	Ghrelin（ng/mL）		IGF-1（ng/mL）	
		Before treatment	After treatment	Before treatment	After treatment
Control group	57	6.45± 0.73	5.32± 0.69*	97.72± 11.21	248.28± 32.33*
Experimental group	57	6.43± 0.81	3.95± 0.47*	97.45± 10.32	379.39± 43.57*
t		0.138	12.389	0.134	18.245
P		0.890	0.000	0.894	0.000

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

2.3 两组患儿治疗后不良反应发生情况

实验组治疗期间 1 例患儿出现血清谷丙转氨酶异常，停药后恢复正常；2 例患儿出现注射皮肤局部红肿，未予处理自行消失；实验组不良反应发生率为 5.26%（3/57）。对照组患儿未见明显不良反应，对照组不良反应发生率为 0.00%（0/57），两组患儿治疗期间不良反应发生情况比较差异无统计学意义（x^2=3.081，*P*=0.079）。

3 讨论

ISS 发病机制复杂，多数患儿除身材矮小外无其他异常症状[13]。ISS 所带来的身材矮小易使患儿自信心缺乏，随着年龄的增长则会出现心理障碍、求职受挫、生活消极等一系列现象[14,15]。因此，在儿童早期诊治中寻求有效的治疗方式，已成为儿科医师的关注热点。有学者研究表明[16]，ISS 的发生与发展可能与生长激素分泌不足有一定关系。生长激素由腺垂体细胞分泌，具有促进骨骼和肌肉生长以及调节内分泌系统的作用，从而改善机体生长速度[17]。rhGH 是一种外源性生长激素，可发挥与生长激素类似的作用，临床多用于生长激素分泌不足的相关疾病中治疗[18]。有研究表明[19]，适量的 rhGH 可改善 ISS 患儿的最终成人身高。这可能与血清中 Ghrelin 、IGF-1 水平的作用机制有关。Ghrelin 是一种含有 28 个氨基酸的脑 - 肠肽，多由胃粘膜细胞分泌，Ghrelin 的主要作用机制是促进生长激素分泌，同时可调节肠胃，参与能量平衡[20]，影响机体生长发育[21]。IGF-1 是一种胰岛素多肽，多数由肝脏细胞分泌，可促进机体细胞生长、分化[22]。Grimberg A 等研究结果表明[23]，ISS 患儿普遍存在血清 IGF-1 水平较低现象，导致患儿降低生长动力，引发生长迟缓，最终致使身材矮小。因此，在临床治疗 ISS 患儿的过程中，应时刻做好上述指标的检测记录，并做出相应的干预处理。

本次研究结果表明，治疗后两组患儿身高、生长速率均较治疗前升高，且实验组高于对照组（*P<0.05*），治疗后两组患儿体重、总甲状腺素、骨龄、空腹血糖水平等较治疗前比较差异无统计学意义（*P>0.05*）。提示 rhGH 治疗 ISS 患儿效果显著，可有效改善患儿身高，加快生长速率，这与赵强等研究结果一致[24]。这主要是由于通过补充 rhGH，可刺激靶细胞产生 IGF-1，从而介导骨骼生长，且 IGF-1 水平又可形成负调节，促进垂体分泌生长激素，进一步促进骨骼生长[25]。治疗后体重、总甲状腺素、骨龄、空腹血糖水平均维持在正常水平，表明 rhGH 安全性好，可维持身体各项正常机能。研究结果还显示，治疗后两组患儿 Ghrelin 水平较治疗前降低，且实验组低于对照组，IGF-1 水平较治疗前升高，且实验组高于对照组（*P<0.05*）。提示经过 rhGH 治疗的 ISS 患儿可明显改善血清 Ghrelin 、IGF-1 水平，从而促进患儿生长。究其原因，笔者认为在 ISS 患儿中，血清 Ghrelin 水平的异常升高，导致血清 Ghrelin 不能正常的促进生长激素分泌。而在使用 rhGH 治疗以后，血清 Ghrelin 水平恢复到正常范围，且以负反馈模式对儿童的发育以及营养状态进行调节作用。又因 rhGH 的作用机制与生长激素类似，由于生长激素的作用发挥离不开血清 IGF-1，生长激素通过刺激血清 IGF-1 的产生，从而发挥促进骨骼生长、调节机体代谢、促进蛋白质合成等作用[26,27]。正常儿童中血清 IGF-1 水平较稳定，其变化主要随生长激素而变化，因此，除外周靶器官异常等情况，血清 IGF-1 水平在 ISS 患儿治疗效果中意义重大[28]。这在曾婷等研究结果中可以加以佐证[29,30]。同时本研究还表明两组患儿治疗期间不良反应发生情况比较差异无统计学意义（*P>0.05*），提示在 ISS 患儿的治疗过程中，rhGH 对身体各方面机能影响不大，安全无副作用。

综上所述，在 ISS 患儿中使用 rhGH 治疗，效果显著，可提高患儿血清 IGF-1 水平，同时改善血清 Ghrelin 水平，且无不良副作用产生，临床具有积极的指导意义，值得推广。

参 考 文 献（References）

[1] Kang MJ. Novel genetic cause of idiopathic short stature [J]. Ann Pediatr Endocrinol Metab, 2017, 22(3): 153-157

[2] Hauer NN, Sticht H, Boppudi S, et al. Genetic screening confirms heterozygous mutations in ACAN as a major cause of idiopathic short stature[J]. Sci Rep, 2017, 7(1): 12225

[3] 干冬梅,石小军.重组人生长激素对特发性矮小患儿症血清胰岛素样生长因子 1 与胰岛素样生长因子结合蛋白 3 水平的影响 [J].中国生化药物杂志, 2015, 35(12): 51-53
Gan Dong-mei, Shi Xiao-jun. Effect of recombinant human growth hormone on serum levels of insulin like growth factor 1 and insulin-like growth factor binding protein 3 in children with idiopathic short stature [J]. Chinese Journal of Biochemical Pharmaceutics, 2015, 35(12): 51-53

[4] Dávid A, Butz H, Halász Z, et al. The prevalence of SHOX gene deletion in children with idiopathic short stature. A multicentric study [J]. Orv Hetil, 2017, 158(34): 1351-1356

[5] Im M, Kim YD, Han HS. Effect of growth hormone treatment on children with idiopathic short stature and idiopathicgrowth hormone deficiency[J]. Ann Pediatr Endocrinol Metab, 2017, 22(2): 119-124

[6] Dias C, Giordano M, Frechette R, et al. Genetic variations at the human growth hormone receptor (GHR) gene locus are associated withidiopathic short stature [J]. J Cell Mol Med, 2017, 21 (11): 2985-2999

[7] Grimberg A, Allen DB. Growth hormone treatment for growth hormone deficiency and idiopathic short stature: new guidelines shaped by the presence and absence of evidence[J]. Curr Opin Pediatr, 2017, 29(4): 466-471

[8] 路宇,于立君,李国庆,等.重组人生长激素治疗生长激素缺乏症的疗效观察[J].现代生物医学进展, 2012, 12(28): 5494-5496
Lu Yu, Yu Li-jun, Li Guo-qing, et al. The Therapeutic Effect of Recombinant Growth Hormone in Children of Growth Hormone Deficient [J]. Progress in Modern Biomedicine, 2012, 12 (28): 5494-5496

[9] Gesmundo I, Miragoli M, Carullo P, et al. Growth hormone-releasing hormone attenuates cardiac hypertrophy and improves heart function in pressure overload-induced heart failure [J]. Proc Natl Acad Sci USA, 2017, 114(45): 12033-12038

[10] Shu X, Feng J, Feng J, et al. Combined delivery of bone morphogenetic protein-2 and insulin-like growth factor-1 from nano-poly (γ-glutamic acid)/β-tricalcium phosphate-based calcium phosphate cement and its effect on bone regeneration in vitro [J]. J Biomater Appl, 2017, 32(5): 547-560

[11] Stawerska R, Czkwianianc E, Smyczyńska J, et al. Nutritional Status in Short Stature Children Is Related to Both Ghrelin and Insulin-like Growth Factor I Concentrations [J]. J Pediatr Gastroenterol Nutr, 2017, 64(5): 812-817

[12] 李嫔. 生长激素受体基因异常及多态性与特发性矮小的关系研究进展[J].中华实用儿科临床杂志, 2014, 29(20): 1523-1525
Li Pin. Progress of association between gene mutations, polymorphisms of growth hormone receptor and idiopathic short stature [J]. Journal of Applied Clinical Pediatrics, 2014, 29 (20): 1523-1525

[13] Del Águila C, Ortiz C, Yarlequé M, et al. GHRd3 polymorphism of growth hormone receptor gen in peruvian children with idiopathic short stature[J]. Rev Peru Med Exp Salud Publica, 2016, 33(1): 45-50

[14] Dateki S, Nakatomi A, Watanabe S, et al. Identification of a novel heterozygous mutation of the Aggrecan gene in a family with idiopathicshort stature and multiple intervertebral disc herniation[J]. J Hum Genet, 2017, 62(7): 717-721

[15] 任翼,陈江,谭志团,等.重组人生长激素治疗特发性矮小症和生长激素缺乏症的比较[J].广东医学, 2016, 37(19): 2961-2963
Ren Yi, Chen Jiang, Tan Zhi-tuan, et al. Comparison of recombinant human growth hormone in the treatment of idiopathic dwarfism and growth hormone deficiency[J]. Guangdong Medical Journal, 2016, 37 (19): 2961-2963

[16] 张萍萍, 方洁. 生长激素对特发性矮小症儿童血清 Ghrelin、LP、IGF-1、IGFBP3 表达水平的影响 [J]. 中国生化药物杂志, 2017, 37 (2):177-179
Zhang Ping-ping, Fang Jie. Effects of growth hormone on serum levels of Ghrelin, LP, IGF-1 and IGFBP3 in children with idiopathic short stature[J]. Chinese Journal of Biochemical Pharmaceutics,2017, 37(2): 177-179

[17] Meazza C, Elsedfy HH, Khalaf RI, et al. Serum α-klotho levels are not informative for the evaluation of growth hormone secretion in shortchildren [J]. J Pediatr Endocrinol Metab, 2017, 30 (10): 1055-1059

[18] Ballerini MG, Braslavsky D, Scaglia PA, et al. Circulating IGF-I, IGFBP-3 and the IGF-I/IGFBP-3 Molar Ratio Concentration and Height Outcome in Prepubertal Short Children on rhGH Treatment over Two Years of Therapy [J]. Horm Res Paediatr, 2017, 88 (5): 354-363

[19] 熊慧,陈红珊,杜敏联,等.生长激素联合司坦唑醇治疗对 Turner 综合征女童成年身高的影响[J].中华实用儿科临床杂志, 2015, 30(8): 623-626
Xiong Hui, Chen Hong-shan, Du Min-lian, et al. The major factors for improving final adult height in girls with Turner syndrome treated with recombinant human growth hormone and Stanazolol [J]. Journal of Applied Clinical Pediatrics, 2015, 30(8): 623-626

[20] Esener OBB, Gurel-Gurevin E, Isbilen-Basok B, et al. Spirulina Platensis Affects Factors Involved in Spermatogenesis and Increases Ghrelin Receptors in Testis Tissue of Rats Fed a High-Fat Diet[J]. Pol J Vet Sci, 2017, 20(3): 467-475

[21] Papandreou D, Karavolias C, Arvaniti F, et al. Fasting Ghrelin Levels Are Decreased in Obese Subjects and Are Significantly Related With Insulin Resistance and Body Mass Index [J]. Open Access Maced J Med Sci, 2017, 5(6): 699-702

[22] Wen YY, Liu WT, Sun HR, et al. IGF-1-mediated PKM2/β-catenin/miR-152 regulatory circuit in breast cancer [J]. Sci Rep, 2017, 7(1): 15897

[23] Grimberg A, DiVall SA, Polychronakos C, et al. Guidelines for Growth Hormone and Insulin-Like Growth Factor-I Treatment in Children and Adolescents: Growth Hormone Deficiency, Idiopathic Short Stature, and Primary Insulin-Like Growth Factor-I Deficiency [J]. Horm Res Paediatr, 2016, 86(6): 361-397

[24] 赵强,李志洁.重组人生长激素治疗儿童生长激素缺乏症和特发性矮小症 45 例疗效观察[J].中国妇幼保健, 2016, 31(6): 1300-1302
Zhao Qiang, Li Zhi-jie. Therapeutic effect of recombinant human growth hormone in 45 children with growth hormone deficiency and idiopathic dwarfism [J]. Maternal & Child Health Care of China, 2016, 31(6): 1300-1302

[25] Fantini C, Sgrò P, Pittaluga M, et al. Short-term, supra-physiological rhGH administration induces transient DNA damage in peripheral lymphocytes of healthy women [J]. J Endocrinol Invest, 2017, 40(6): 645-652

[26] Tian F, Liu GR, Li N, et al. Insulin-like growth factor I reduces the occurrence of necrotizing enterocolitis by reducing inflammatory response and protecting intestinal mucosal barrier in neonatal rats model[J]. Eur Rev Med Pharmacol Sci, 2017, 21(20): 4711-4719

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[13] Usuda K, Maeda S, Motomo N, et al. Pulmonary Function After Lobectomy: Video-Assisted Thoracoscopic Surgery Versus Muscle-Sparing Mini-thoracotomy[J]. Indian J Surg, 2017, 79(6): 504-509

[14] Yu Z, Xie Q, Guo L, et al. Perioperative outcomes of robotic surgery for the treatment of lung cancer compared to a conventional video-assisted thoracoscopic surgery? (VATS) technique [J]. Oncotarget, 2017, 8(53): 91076-91084

[15] Li L, Jin J, Min S, et al. Correction: Compliance with the enhanced recovery after surgery protocol and prognosis aftercolorectal cancer surgery: A prospective cohort study [J]. Oncotarget, 2017, 8 (52): 90605

[16] Bray MS, Appel AL, Kallies KJ, et al. Implementation of an Enhanced Recovery After Surgery Program for Colorectal Surgery at a Community Teaching Hospital[J]. WMJ, 2017, 116(1): 22-26

[17] Paduraru M, Ponchietti L, Casas IM, et al. Enhanced Recovery After Surgery (ERAS) - The Evidence in Geriatric Emergency Surgery: A Systematic Review[J]. Chirurgia (Bucur), 2017, 112(5): 546-557

[18] Pache B, Hübner M, Jurt J, et al.Minimally invasivesurgery and enhanced recovery after surgery: The ideal combination? [J]. J Surg Oncol, 2017, 116(5): 613-616

[19] Segelman J, Nygren J. Best practice in major elective rectal/pelvic surgery: enhanced recovery after surgery (ERAS) [J]. Updates Surg, 2017, 69(4): 435-439

[20] Brandal D, Keller MS, Lee C, et al. Impact of Enhanced Recovery After Surgery and Opioid-Free Anesthesia on Opioid Prescriptions at Discharge From the Hospital: A Historical-Prospective Study [J]. Anesth Analg, 2017, 125(5): 1784-1792

[21] Zhou J, He Q, Wang J, et al. Application of Enhanced Recovery After Surgery in Single-incision Laparoscopic Distal Gastrectomy [J]. Surg Laparosc Endosc Percutan Tech, 2017, 27(6): 449-455

[22] McGrath JS, Pruthi RS. Surgery: Enhanced recovery after cystectomy: cocktails, culture, or consistency? [J]. Nat Rev Urol, 2017, 14(11): 648-649

[23] Vendler MMI, Haidari TA, Waage JE, et al. Incidence of venous thromboembolic events in enhanced recovery after surgery for colon cancer: a retrospective, population-based cohort study [J]. Colorectal Dis, 2017, 19(11): O393-O401

[24] Kidane B. A rose by any other name: Marginal gains of enhanced recovery after surgery in video-assisted thoracic surgery perioperative care[J]. J Thorac Cardiovasc Surg, 2017, 154(6): 2082-2083

[25] Zainfeld D, Djaladat H. Enhanced recovery after urologic surgery-Current applications and future directions[J]. J Surg Oncol, 2017, 116 (5): 630-637

[26] Damania R, Cocieru A. Impact of enhanced recovery after surgery protocols on postoperative morbidity and mortality in patients undergoing routine hepatectomy: review of the current evidence [J]. Ann Transl Med, 2017, 5(17): 341

[27] Jones D, Musselman R, Pearsall E, et al. Ready to Go Home Patients' Experiences of the Discharge Process in an Enhanced Recovery After Surgery (ERAS) Program for Colorectal Surgery [J]. J Gastrointest Surg, 2017, 21(11): 1865-1878

[28] Leeds IL, Alimi Y, Hobson DR, et al. Racial and Socioeconomic Differences Manifest in Process Measure Adherence for EnhancedRecovery After Surgery Pathway [J]. Dis Colon Rectum, 2017, 60(10): 1092-1101

[29] Herbert G, Sutton E, Burden S, et al. Healthcare professionals' views of the enhanced recovery after surgery programme: a qualitative investigation[J]. BMC Health Serv Res, 2017, 17(1): 617

[30] Powell AC, Stopfkuchen-Evans M, Urman RD, et al. Decreasing the Surgical Stress Response and an Initial Experience from the Enhanced RecoveryAfter Surgery Colorectal Surgery Program at an Academic Institution[J]. Int Anesthesiol Clin, 2017, 55(4): 163-178

（上接第 3857 页）

[27] García-Marchena N, Silva-Peña D, Martín-Velasco AI, et al. Decreased plasma concentrations of BDNF and IGF-1 in abstinent patients with alcohol use disorders [J]. PLoS One, 2017, 12 (11): e0187634

[28] Xu Y, Liu MC, Wang P, et al. Correlation between serum IGF-1 and blood lead level in short stature children and adolescent with growth hormone deficiency[J]. Int J Clin Exp Med, 2014, 7(4): 856-864

[29] 曾婷,李红辉,严提珍,等.柳州市特发性矮小症瑶族学龄儿童维生素 D 和 IGF-1 水平与体格发育指标的相关性分析[J].职业与健康, 2017, 33(6): 794-796

Zeng Ting, Li Hong-hui, Yan Ti-zhen, et al. Analysis on correlation between levels of Vitamin D and IGF-1 and anthropometric indexes among school-age children of Yao nationality with idiopathic short stature in Liuzhou[J]. Occupation and Health, 2017, 33(6): 794-796

[30] Cieszkowski J, Warzecha Z, Ceranowicz P, et al. Therapeutic effect of exogenous ghrelin in the healing of gingival ulcers is mediated by the release of endogenous growth hormone and insulin-like growth factor-1[J]. J Physiol Pharmacol, 2017, 68(4): 609-617