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重度烧伤患者应用重组人生长激素治疗的临床效果*

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摘要 目的:研究重组人生长激素对重度烧伤的应用治疗效果。**方法:**选取重度烧伤患者 42 例。根据随机数表法,将所有患者分为观察组(n=21)和对照组(n=21),观察组在对照组的基础上给予重组人生长激素治疗。**结果:**对照组术后 24 h 血红蛋白及总蛋白水平平均低于实验组,差异无统计学意义($P>0.05$);对照组术后 1 周血红蛋白水平为(95.57 ± 11.41)g/L,低于实验组的(137.91 ± 14.29)g/L($t=3.726, P<0.001$);对照组术后 2 周血红蛋白水平为(80.89 ± 11.38)g/L,低于实验组的(131.28 ± 13.47)g/L($t=3.917, P<0.001$);实验组术后 1 周总蛋白水平为(61.47 ± 5.19)g/L,高于对照组的(39.18 ± 2.76)g/L($t=3.927, P<0.001$);实验组术后 2 周总蛋白水平为(55.78 ± 6.38)g/L,高于对照组的(36.81 ± 5.17)g/L($t=3.847, P<0.001$)。实验组术后 24h 的 TNF- α 和 IL-6 高于对照组,差异无统计学意义($P>0.05$);实验组术后 2 周的 TNF- α 、IL-6 均明显低于对照组,差异有统计学意义($P<0.001$);实验组术后 2 周的 TNF- α 、IL-6 均明显低于对照组,差异有统计学意义($P<0.001$);观察组的住院时长为(47.82 ± 7.46)天,显著低于对照组的(79.36 ± 8.10)天($t=4.275, P<0.001$);观察组的供皮区、植皮区、深 II 度痂下愈合时间均显著低于对照组的,差异有统计学意义($P<0.001$)。**结论:**rhGH 对重度烧伤的疗效非常显著,值得在临床中推广。

关键词:重组人生长激素;重度烧伤;免疫机制;血浆蛋白

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Clinical Effect of Recombinant Human Growth Hormone Therapy in Patients with Severe Burn*

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ABSTRACT Objective: To study the effect of recombinant human growth hormone on the treatment of severe burn. **Methods:** 42 cases of severe burn patients in our hospital from February 2013 to December 2015 were divided into observation group (n=21) and control group (n=21) according to the random number table method. Patients in the observation group was given recombinant human growth hormone therapy on the basis of the control group. **Results:** At postoperative 24h, the hemoglobin and total protein levels were lower in the control group than in the experimental group, but the difference was not statistically significant ($P>0.05$). After one week, the hemoglobin level of control group was(95.57 ± 11.41)g/L, lower than that of experimental group (137.91 ± 14.29)g/L ($t=3.726, P<0.001$). After 2 weeks, the hemoglobin level of control group was(80.89 ± 11.38)g/L, lower than that of experimental group (131.28 ± 13.47) g/L ($t=3.917, P<0.001$). As for the total protein level, it was (61.47 ± 5.19) g/L in the experimental group after 1 weeks, higher than (39.18 ± 2.76) g/L in the control group ($t=3.927, P<0.001$). Yet it was still higher in the experimental group [55.78 ± 6.38] g/L after 2 weeks than in the control group [36.81 ± 5.17] g/L [$t=3.847, P<0.001$]. The experimental group had higher TNF- α and IL-6 levels than the control group after 24h, but the difference was not statistically significant ($P>0.05$). At 2 weeks after surgery, the TNF- α and IL-6 levels in the experimental group were significantly lower than in the control group, the difference was statistically significant ($P<0.001$). The length of hospitalization in the experimental group was (47.82 ± 7.46) days, significantly shorter than in the control group [79.36 ± 8.10 days] ($t=4.275, P<0.001$). The healing time of the graft area, donor skin and deep second degree under the scab were significantly shorter in the experimental group than in the control group, and the difference was statistically significant ($P<0.001$). **Conclusion:** RhGH is significant in the treatment of severe burns, so it is worth promoting in clinic.

Key words: Recombinant human growth hormone; Severe burn; Immune mechanism; Plasma protein

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前言

烧伤带来的影响不仅为皮肤创伤和炎症反应,对机体的代谢紊乱只是其中一个并发症,更严重的是对内脏的损伤,对患者造成更大的痛苦。在机体受到烧伤之后首要的任务为手术治疗,在手术后应加快对创面愈合,使得高代谢反应减轻^[1]。生长素对人体的蛋白质的合成具有促进作用,重组人生长素(Recombinant human growth hormone, rHGH)可激活机体免疫系统,调节内分泌系统,从而有利于机体蛋白质的加速合成^[2]。使用 rHGH 在现代烧伤治疗中为常用方案,现研究重度烧伤患者应用 rHGH,检验 rHGH 的实际疗效。

1 资料与方法

1.1 一般资料

选取我院 2013 年 2 月至 2015 年 12 月住院部重度烧伤患者 42 例,其中男性 31 例,女性 11 例,年龄为 24-49 岁,平均年龄为 (34.62 ± 8.90) 岁。纳入标准^[3]:1)烧伤面积为 30%~70%;2)III度烧伤面积 > 10%。排除标准^[4]:1)伴随肝肾衰竭;2)伴随全身性免疫疾病;3)存在药物过敏史。根据随机数表法,将所有患者分为观察组(n=21)和对照组(n=21),两组在年龄分布、性别比例及烧伤程度等方面差异无统计学意义($P>0.05$)。实验经院伦理协会批准,且均获得患者知情同意书签字。

1.2 主要仪器与试剂

全自动生化分析仪(宝石 GEM3000,美国),rHGH(安徽安科生物工程(集团)股份有限公司生产,批号:20130807)。

1.3 方法

两组均进行外科手术治疗,术后给予抗感染治疗及营养支

持。此外观察组额外给予 rHGH,用量为 $0.1 \text{ mg} \cdot \text{kg}^{-1}$,1 次/d,对照组给予 0.9% NaCl $0.1 \text{ mg} \cdot \text{kg}^{-1}$,1 次/d,两组均采用皮下注射^[5]。药物治疗为期 2 周。

1.4 观察指标

分别在术后 24 小时内、治疗 1 周、术后 2 周三个时间抽取患者空腹静脉血,使用全自动生化分析仪进行检查,记录患者血浆中总蛋白和血红蛋白水平,使用 ELASA 法^[6]并记录细胞中免疫因子水平,包括 TNF- α , IL-6。此外记录并统计两组患者住院时长及供皮区、植皮区和深 II 度痂下愈合所需时间。

1.5 统计学方法

计数资料行 χ^2 检验或确切概率法,计量资料用 $(\bar{x} \pm s)$ 表示,组间比较采用两样本 t 检验,如结果提示 $P<0.05$,差异存在统计学意义。

2 结果

2.1 两组不同时间血红蛋白、血浆总蛋白变化比较

对照组术后 24h 血红蛋白水平低于实验组,差异无统计学意义($t=0.692, P=0.217$);对照组术后 1 周血红蛋白水平为 $(95.57 \pm 11.41) \text{ g/L}$,低于实验组的 $(137.91 \pm 14.29) \text{ g/L}$,差异有统计学意义($t=3.726, P<0.001$);对照组术后 2 周血红蛋白水平为 $(80.89 \pm 11.38) \text{ g/L}$,低于实验组的 $(131.28 \pm 13.47) \text{ g/L}$,差异有统计学意义($t=3.917, P<0.001$);实验组术后 24h 总蛋白水平高于对照组,差异无统计学意义($t=0.839, P=0.107$);实验组术后 1 周总蛋白水平为 $(61.47 \pm 5.19) \text{ g/L}$,高于对照组的 $(39.18 \pm 2.76) \text{ g/L}$,差异有统计学意义($t=3.927, P<0.001$);实验组术后 2 周总蛋白水平为 $(55.78 \pm 6.38) \text{ g/L}$,高于对照组的 $(36.81 \pm 5.17) \text{ g/L}$,差异有统计学意义($t=3.847, P<0.001$)(表 1)。

表 1 两组不同时间血红蛋白、血浆总蛋白变化比较($\text{g/L}, \bar{x} \pm s$)

Table 1 Comparison of hemoglobin and plasma total protein at different time between two groups($\text{g/L}, \bar{x} \pm s$)

Groups	Cases	Postoperative 24 h		Postoperative 1 w		Postoperative 2 w	
		Hemoglobin	Total protein	Hemoglobin	Total protein	Hemoglobin	Total protein
Control group	21	176.35 ± 10.82	36.80 ± 6.10	95.57 ± 11.41	39.18 ± 2.76	80.89 ± 11.38	36.81 ± 5.17
Experimental group	21	179.01 ± 11.83	37.39 ± 7.49	137.91 ± 14.29	61.47 ± 5.19	131.28 ± 13.47	55.78 ± 6.38
t		0.692	0.839	3.726	3.927	3.917	3.847
P		0.217	0.107	<0.001	<0.001	<0.001	<0.001

2.2 对比两组不同时间 TNF- α , IL-6 的结果

实验组术后 24h 的 TNF- α 高于对照组,差异无统计学意义($t=0.592, P=0.205$);实验组术后 24h 的 IL-6 高于对照组,差异无统计学意义($t=0.965, P=0.091$);实验组术后 1 周的 TNF- α 为 $(18.54 \pm 3.73) \text{ ng/L}$,低于对照组的 $(24.82 \pm 7.10) \text{ ng/L}$,差异具有统计学意义($t=3.872, P<0.001$);实验组术后 2 周的 TNF- α 为 $(15.28 \pm 3.51) \text{ ng/L}$,低于对照组的 $(25.36 \pm 4.89) \text{ ng/L}$,差异具有统计学意义($t=4.018, P<0.001$);实验组术后 1 周的 IL-6 为 $(134.63 \pm 67.38) \text{ ng/L}$,低于对照组的 $(273.71 \pm 88.02) \text{ ng/L}$,差异具有统计学意义($t=4.827, P<0.001$);实验组术后 2 周的 IL-6 为 $(90.83 \pm 20.47) \text{ ng/L}$,低于对照组的 $(208.64 \pm 63.27) \text{ ng/L}$,差异具有统计学意义($t=4.781, P<0.001$)(表 2)。

2.3 对比两组创伤愈合时间、住院时长

观察组的住院时长为 (47.82 ± 7.46) 天,显著低于对照组的 (79.36 ± 8.10) 天,差异有统计学意义($t=4.275, P<0.001$);观察组的供皮区愈合时间为 (8.29 ± 1.38) 天,明显低于对照组的 (12.73 ± 2.01) 天,差异有统计学意义($t=3.482, P<0.001$);观察组的植皮区愈合时间为 (30.47 ± 8.27) 天,显著低于对照组的 (48.29 ± 7.31) 天,差异有统计学意义($t=3.957, P<0.001$);观察组的深 II 度痂下愈合时间为 (19.47 ± 3.74) 天,显著低于对照组的 (29.37 ± 7.39) 天,差异有统计学意义($t=4.968, P<0.001$)(表 3)。

3 讨论

烧伤对人体组织破坏性极大,重度烧伤患者的免疫系统受到破坏,可引起全身性免疫疾病,造成创口的感染和发热^[6,7]。同时烧伤导致血液 PH 值下降,使得血液组织相继出现缺氧,从

而坏死。重度烧伤患者甚至出现器官衰竭,造成体内激素失衡、蛋白质加速分解等机体紊乱情况,当蛋白质分解过多,机体长期处于负氮平衡状态将促进蛋白质分解,使得患者体重不断下降,且伤口拖延难以愈合,甚至造成死亡^[8,9]。相关研究表明^[10]烧

伤的治疗原则为早治疗,防感染,重预后。重组人生长激素在临床医学领域应用广泛,国外研究表明^[11]注射重组人生长激素能有效提高重度烧伤患者的恢复,加快内环境的平衡。

表 2 两组不同时间 TNF- α , IL-6 的结果对比 (ng/L, $\bar{x} \pm s$)Table 2 Comparison of the results of TNF- α and IL-6 at different time between two groups (ng/L, $\bar{x} \pm s$)

Groups	Cases	Postoperative 24h		Postoperative 1w		Postoperative 2w	
		TNF- α	IL-6	TNF- α	IL-6	TNF- α	IL-6
Control group	21	27.63 $\pm$ 4.20	577.20 $\pm$ 132.92	24.82 $\pm$ 7.10	273.71 $\pm$ 88.02	25.36 $\pm$ 4.89	208.64 $\pm$ 63.27
Experimental group	21	29.47 $\pm$ 4.84	587.36 $\pm$ 128.67	18.54 $\pm$ 3.73	134.63 $\pm$ 67.38	15.28 $\pm$ 3.51	90.83 $\pm$ 20.47
t		0.592	0.965	3.872	4.827	4.018	4.781
P		0.205	0.091	<0.001	<0.001	<0.001	<0.001

表 3 两组创伤愈合时间、住院时长对比 (d, $\bar{x} \pm s$)

Table 3 Comparison of the wound healing time and the length of stay in hospital between two groups

Groups	Cases	Wound healing time			Length of stay
		Donor site	The graft area	Deep II degree of healing	
Control group	21	12.73 $\pm$ 2.01	48.29 $\pm$ 7.31	29.37 $\pm$ 7.39	79.36 $\pm$ 8.10
Experimental group	21	8.29 $\pm$ 1.38	30.47 $\pm$ 8.27	19.47 $\pm$ 3.74	47.82 $\pm$ 7.46
t		3.482	3.957	4.968	4.275
P		<0.001	<0.001	<0.001	<0.001

根据实验数据表明对照组术后 24h 血红蛋白及总蛋白水平平均低于实验组,差异无统计学意义 ($P>0.05$);对照组术后 1 周和术后 2 周血红蛋白水平和总蛋白水平低于实验组,差异有统计学意义 ($P<0.001$)。rhGH 能有效恢复血浆蛋白的生成,加快血液功能的恢复。实验组和对照组在术后 24h 的 TNF- α 、IL-6 差别无统计学意义 ($P>0.05$),在术后 1 周和术后 2 周实验组的 TNF- α 、IL-6 均显著低于对照组,表明 rhGH 的疗效非常快速,能在短期快速调整体内免疫机制,缩短伤口肿胀热痛的时间。此外,实验组的创伤愈合时间和住院时长均显著低于对照组,数据再一次证实注射 rhGH 能加快患者机体的恢复,在血液及免疫系统各方面均发挥较大作用。

烧伤在临床分为三度^[12,13]: I 度为表皮层,红肿热痛,小水泡,不落疤痕,七天左右痊愈;浅 II 度为表皮层,红肿热痛,大水泡,直达真皮,不落疤痕,十四天左右痊愈;深 II 度为真皮层损伤,真皮、肌肉伤处有结甲渗出一层,落轻度疤痕,二十至三十天可痊愈;III 度为肌肉骨骼,伤及达骨骼,渗出少,难痊愈,落疤痕,面积大的易得败血症可危及生命,俩月以上痊愈。深 II 度烧伤即可以对脏器造成损伤,III 度为危重症,往往造成患者术后感染或功能不及而死亡, rhGH 对 III 度烧伤的关键性不言而喻。而 rhGH 为 191 个氨基酸残基或 N 端有一甲硫氨酸的 192 个氨基酸残基组成的蛋白,具备调整内分泌系统、激活并维护免疫系统的正常工作等作用^[14-17]。在研究还发现^[18] rhGH 的其他作用,包括激活细胞的活性电子、振荡分子,使停止分裂的皮肤底层细胞再生长,促进伤口的愈合,减少局部水肿和疤痕的形成,使得烧伤皮肤可提早愈合。此外 rhGH 可促进肌肉生长,促进心、肝、肾、胰岛等脏腑细胞的再生,减少蛋白质分解和内脏受损对机体带来的负荷^[19,20]。

综上所述, rhGH 对重度烧伤的疗效非常显著,能调整机体免疫系统,加速血浆蛋白的再生,降低患者的住院时间,为患者经济和心理带来福音,值得在临床中推广。

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