

doi: 10.13241/j.cnki.pmb.2014.07.028

# VSD 联合金因肽治疗手足外科难愈性伤口的临床研究

罗洪斌 韦昌南 钱爱莲 冯兴伦 邓洁梅

(佛山市中医院三水医院 广东 佛山 528100)

**摘要 目的:**观察封闭式负压引流技术(VSD)联合金因肽治疗手足外科难愈性伤口的临床疗效,为临床联合运用提供依据。**方法:**86例手足外科难愈性伤口患者随机分为治疗组和对照组各43例,治疗组采用VSD联合金因肽治疗,对照组采用常规换药治疗,观察两组临床疗效和上皮化时间、愈合时间、创面愈合率、换药次数、伤口疼痛评分、住院费用差异。**结果:**治疗组总有效率90.70%;对照组总有效率72.09%;两组比较,有显著性差异( $P < 0.05$ );治疗组上皮化时间、愈合时间、创面愈合率、换药次数、伤口疼痛评分、住院费用较对照组相比明显缩短,差异有统计学意义( $P < 0.05$ )。**结论:**VSD联合金因肽治疗手足外科难愈性伤口疗效确切,能更好促进损伤组织的修复,加速创面愈合,值得临床推广应用。

**关键词:** VSD; 金因肽; 手足外科; 难愈性伤口

**中图分类号:** R605 **文献标识码:** A **文章编号:** 1673-6273(2014)07-1312-03

## Clinical Research of VSD Combined with RhEGF on Treating Refractory Wounds of the Foot Surgery

LUO Hong-bin, WEI Chang-nan, QIAN Ai-lian, FENG Xing-lun, DENG Jie-mei

(Sanshui Branch of Foshan Hospital of Traditional Chinese Medicine, Foshan, Guangdong, 528100, China)

**ABSTRACT Objective:** To study the clinical research of Vacuum Sealing Drainage combined with rhEGF on treating refractory wounds of the hand and foot surgery, to provide basis for clinical joint use. **Methods:** 86 patients were randomly divided into treatment group 43 cases and 43 cases of control group, the treatment group were treated by VSD combined with rhEGF, while the control group were treated with conventional dressing, the efficacy and the difference of epithelialization time, healing time, wound healing rate, number of switches, wound pain score, hospitalization expenses of two groups were observed. **Result:** The total effective rate of the treatment group was 90.70%, the control group was 72.09%, the two groups in clinical curative effect had significant difference ( $P < 0.05$ ); the epithelialization time, healing time, wound healing rate, number of switches, wound pain score, hospitalization expenses were reduced in treatment group than those in the control group ( $P < 0.05$ ). **Conclusion:** VSD combined rhEGF had definite effect for refractory wounds of the foot surgery, which could better promote tissue damage repair, accelerating wound healing, it is worthy of clinical application.

**Key words:** VSD; rhEGF; Hand and Foot surgery; Refractory wounds

**Chinese Library Classification(CLC):** R605 **Document code:** A

**Article ID:** 1673-6273(2014)07-1312-03

### 前言

封闭式负压引流技术(Vacuum Sealing Drainage, VSD)是由德国 Neischman 博士于1992年首创的一种伤口治疗的全新方法,其原理是利用负压吸引装置与特殊创面敷料连接,间歇地或持续地在创面处产生低于大气压的压力,将引流区内的渗出物和坏死组织及时清除,同时有利于局部微循环的改善和组织水肿的消退,刺激肉芽组织的生长,加快组织的修复。该方法最先应用于骨科领域治疗软组织缺损和感染性创面,目前已被广泛应用于急、慢性创面,是骨科和外科领域的革命<sup>[1]</sup>。手及足部皮肤缺损及糖尿病足等所致难愈性伤口或创面是手足外科面临的难题。有研究表明,VSD可有效治疗手足外科难愈性伤口或创面,但相关临床研究甚少。此外,表皮生长因子是目前已知

能发挥诱导和刺激创面细胞增殖、维持细胞存活等生物效应的一类极其重要的蛋白类物质,临床广泛用于创口愈合,但两者联合运用治疗手足外科难愈性伤口能否发挥增效作用,目前未见报道。本研究旨在观察VSD联合金因肽治疗手足外科难愈性伤口或创面的疗效,并与常规换药对比,以观察二者联合能否更好促进伤口的愈合,现报告如下。

### 1 资料与方法

#### 1.1 一般资料

选择我院手足外科门诊和住院部2011年5月~2013年5月间难愈性伤口患者共计86例。纳入标准:①各种外伤导致的慢性皮肤伤口持续达1个月以上者,久治不愈或者持续恶化,皮肤创面最小直径大于3cm;②未采用VSD治疗者;③常规清创换药7d后,创面仍未好转者;④创面污染较重,或经常规换药后无效。排除标准:①合并严重心脑血管、肝肾、造血系统的患者,或无法耐受手术者;②软组织恶性肿瘤,免疫性疾病,

作者简介:罗洪斌(1978-),男,学士,主治医师,主要研究方向:手足外科,电话:13719311111, E-mail: Luohongbin2008@126.com

(收稿日期:2013-06-17 接受日期:2013-07-18)

使用免疫抑制剂、糖皮质激素及化学治疗药物,低蛋白症,中度或重并贫血;③经常规换药后有效,或慢性创面有活动性出血。86例患者随机分为治疗组和对照组各43例。治疗组男26例,女17例,年龄34~69岁,平均年龄(45.54±6.28)岁;对照组男29例,年龄女14例,年龄33~67岁,平均年龄(46.33±5.46)岁。两组性别、年龄等资料经统计学处理,无显著差异( $P>0.05$ )。

### 1.2 材料

①VSD:由武汉维斯第公司生产,内置多侧孔硬质硅胶引流管,且可根据临床需要进行修剪;②英国施乐辉公司生产的生物半透性薄膜具,主要成分为丙烯酸和聚氨酯;③对流冲洗管;④冲洗液:0.9%生理盐水(四川奇力制药生产);⑤负压源。

### 1.3 方法

两组在常规抗感染基础上,加强对患者的营养支持,并针对基础疾病,联合相关专科医生制定诊疗措施。治疗组在此基础上采用VSD联合金因肽治疗:①常规清理创面,清除创面坏死组织与异物,待创面周围皮肤干燥后,再在创面上喷金因肽,并等待1分钟。②依据患者创面大小和形状,进行修剪、拼接VSD敷料。③VSD敷料与创面充分接触。④采用薄膜黏贴密封创面,贴膜要保证至少达创面外3cm以上,⑤引流管接通负压装置,压力设定为-250mmHg,如引流管较多,可采用多个三通接头将引流管串接至1~2个负压源。⑥7~10d后,依据创面肉芽生长情况进行2次清创植皮或行肌皮瓣转移,对于创面缺损感染较重者通常需要更换1~2次。引流管堵塞者行再通,无法再通者更换VSD。对照组在此基础上进行常规消毒创面,后分别以3%过氧化氢、生理盐水清洗、冲洗创面后,以灭菌敷料

覆盖创面,根据创面渗出情况加用棉垫,并以胶布固定,1天1次。

### 1.4 观察指标

创面愈合时间:分别在皮肤伤口治疗前1d、换药时观察创缘色泽、渗出物、创缘周围皮肤改变,测量创面直径,以mm为单位,观察创面愈合时间(治疗开始至创面完全上皮化)并记录,此外记录治疗期间的换药次数和住院费用,对伤口疼痛评分采用VAS评分<sup>[9]</sup>,分值在0分~10分之间,由病人根据换药期间对两种方法的总体感受分别进行评分。

### 1.5 判断标准

创面修复观察:创面愈合:结痂脱落或皮肤肤色正常;显效:创面缩小80%以上,肉芽及上皮组织生长良好;好转:创面缩小达50%,创面边缘有新的肉芽组织生长,但边缘有少量渗液;无效:治疗前后创面无变化或恶化。采用摄像方格法计算创面愈合率<sup>[9]</sup>。

### 1.6 统计学方法

采用SPSS 12.0统计软件,计量资料以( $\bar{X} \pm S$ )表示,采用 $\chi^2$ 检验进行数据处理。

## 2 结果

### 2.1 两组疗效比较

见表1。治疗组愈合23例,显效9例,好转7例,无效4例,总有效率90.70%;对照组显效14例,好转8例,无效8例;总有效率72.09%;两组比较,有显著性差异( $P<0.05$ )。

表1 两组疗效比较

Table 1 Clinical Comparison of two groups

| Group             | n  | Concrescence | Markedly | Improvement | Invalid | Efficient % |
|-------------------|----|--------------|----------|-------------|---------|-------------|
| Observation group | 43 | 23           | 9        | 7           | 4       | 90.70#      |
| Control group     | 43 | 14           | 8        | 8           | 12      | 72.09       |

注:与对照组比较, # $P<0.05$ 。

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

### 2.2 两组创面开始上皮化时间与创面愈合时间比较

见表2。治疗组上皮化时间、愈合时间较对照组相比,明显

缩短,差异有统计学意义( $P<0.05$ )。

表2 两组创面开始上皮化时间与创面愈合时间比较( $\bar{x} \pm s$ )

Table 2 Comparison of the epithelial change time and healing time in two groups

| Group             | n  | Epithelial change time(d) | Healing time(d) |
|-------------------|----|---------------------------|-----------------|
| Observation group | 43 | 3.65±1.56*                | 4.35±1.54*      |
| Control group     | 43 | 5.65±1.40                 | 6.39±1.68       |

注:与对照组比较, # $P<0.05$ 。

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

### 2.3 两组创面愈合率、换药次数、伤口疼痛评分、住院费用比较

见表3。治疗组创面愈合率、换药次数、伤口疼痛评分、住院费用与对照组比较,差异有统计学意义( $P<0.05$ )。

## 3 讨论

难愈性伤口或创面是指一类与创伤部位和宿主有关的创

面在期望的时间内不能正常愈合<sup>[4]</sup>。本病具有发病机制复杂、治疗难度大、费用高等特点,是临床亟待解决的问题之一,尤其是手足外科治疗的难点<sup>[9]</sup>。伤口愈合是局部组织通过再生、修复、重建进行修补的一系列病理生理过程,这三个时期是可以相互重叠发生的。近年来,促进慢性难愈性伤口的修复是研究的热点之一。既往治疗多采用保守治疗、植皮或截肢术等。但传统换

表3 两组创面愈合率、换药次数、伤口疼痛评分、住院费用比较( $\bar{x} \pm s$ )

Table 3 Comparison of wound healing rate, time of dressing change, score of wound pain, hospitalization costs in two groups

| Group             | n  | Wound healing rate (%) | Time of dressing change | Score of wound pain (grade) | Hospitalization costs (ten thousand) |
|-------------------|----|------------------------|-------------------------|-----------------------------|--------------------------------------|
| Observation group | 43 | 56.65 $\pm$ 7.56*      | 4.35 $\pm$ 1.54*        | 4.65 $\pm$ 1.56*            | 6.96 $\pm$ 1.54*                     |
| Control group     | 43 | 35.53 $\pm$ 1.40       | 6.39 $\pm$ 1.68         | 6.65 $\pm$ 1.40             | 7.67 $\pm$ 1.66                      |

注:与对照组比较, #P&lt;0.05。

Note: Compared with control group, \*P&lt;0.05.

药方法疗效差、疗程长、工作量大,易反复不愈。物理治疗对改善局部血液循环有辅助作用,但由于慢性溃疡患者大多同时合并有全身性疾病。寻求有效的治疗方法已成为医务工作者的共同追求。

VSD是近年来发展起来的一种创面治疗新技术,其原理是利用负压吸引装置与特殊创面敷料连接,间歇地或持续地在创面处产生低于大气压的压力,将引流区内的渗出物和坏死组织及时清除,并有利于改善局部微循环、消退组织水肿、加快肉芽组织的生长,加快组织的修复<sup>[9]</sup>。VSD技术在国外发展已有近20年历史,由德国ULM大学外科医生Fleischmann博士等<sup>[7]</sup>于1992年首创,1997年Argenta及Morykwas的报告为VSD提供了实验和临床依据<sup>[8,9]</sup>。由于VSD使用医用高分子泡沫材料作为负压引流管和创面间的中介,而泡沫材料的高度可塑性,从而使负压可到达被引流区的每一点,形成全方位引流。VSD具有广泛的适应证<sup>[10]</sup>,多项临床研究证实<sup>[11-18]</sup>。VSD治疗各种难愈性伤口或创面具有其优势:促进创面愈合,缩短病程;缩小创面,节约供皮;充分引流,高效引流,控制感染;减轻伤病员痛苦,节约医疗资源。金因肽为外用表皮生长因子,能弥补内源性生长因子量的不足或上调其受体表达,目前利用基因重组技术合成的碱性成纤维细胞生长因子已广泛应用于临床,能促进人皮肤表皮细胞、成纤维细胞和内皮细胞等的生长增殖,显著促进创面上皮化<sup>[19,20]</sup>,但其联合VSD治疗效果如何,目前尚无相关研究报道。

因此,本课题采用VSD联合金因肽治疗手足外科难愈性伤口,并与常规换药为对照,系统观察其对伤口愈合率、愈合时间、换药次数、伤口疼痛等的影响。从本次研究结果显示,治疗组在采用VSD治疗的同时,将促创面愈合药物金因肽配合使用,其能明显的促进多种组织细胞等分化和均衡生长调节作用,促进损伤组织的修复,加速创面愈合,促进血管新生,改善微循环,其临床疗效及相关指标较对照组相比明显缩短,差异有统计学意义(P<0.05)。因此,采用VSD联合金因肽治疗,能更好促进创面愈合,提高临床疗效,对治疗手足外科难愈性伤口具有重要的临床价值,值得临床推广应用。

#### 参考文献(References)

- [1] 刘三凤,刘志豪,戴志波. 负压封闭引流技术(VsD)对各种复杂创面修复的临床研究[J]. 当代医学, 2009, 15(6): 66-68  
Liu San-feng, Liu Zhi-hao, Dai Zhi-bo. Clinical studies of Vacuum-assisted closure (VsD) on a variety of complex wound repair[J]. Contemporary Medicine, 2009, 15(6): 66-68
- [2] Revill SI, Robinson JO, Rosen M. The reliability of a linear analogue for evaluating pain. Anaesthesia, 1976, 31: 1191
- [3] Yinocy J, Aibles JM, Wicke C, et al. Treatment of periprosthetic soft

tissue infection of the groin following vascular surgical procedures by means of a polyvinyl alcohol-vacuum sponge system [J]. Wound Repair Regen, 2003, 11(2): 104-109

- [4] 叶敏. 现代泌尿外科理论与实践[M]. 上海:复旦大学出版社, 2005, 377  
Ye Min. Modern urology theory and practice [M]. Shanghai: Fudan University Press, 2005, 377
- [5] 姜玉峰. 体表慢性难愈合创面的研究进展 [J]. 感染、炎症、修复, 2011, 12(1): 59-61  
Jiang Yu-feng. The research progress of Chronic difficult healing wound surface[J]. Infection, Inflammation; Repair, 2011, 12(1): 59-61
- [6] Kakagia D, Karadimas E, Drosos G, et al. Vacuumassisted closure downgra desreconstructive demands in high-risk patients with severe lower extremity injuries[J]. Acta Chir Plast, 2009, 51(3-4): 59-64
- [7] Fleischmann W, Strecker W, Bombelli M, et al. Vacuum seal ing as treatment of soft tissue damage in open fractures[J]. Unfallchirurg, 1993, 96(9): 488-492
- [8] Morykwas MJ, Argenta LC, Shelton-Brown EI, et al. LC Vaccum-assisted closure: A new method for wound control and treatment: Animal studies and basic foundation[J]. Ann Plast Surg, 1997, 38(6): 553
- [9] Argenta LC, Morykwas MJ. Vacuum-assisted Closure: a new method for wound control and treatment [J]. Clinical Experience. Ann Plast Surg, 1997, 38(6): 563-577
- [10] 裴华德, 宋九宏. 负压封闭引流技术[M]. 2版. 北京:人民卫生出版社, 2008: 3-34  
Qiu Hua-de, Song Jiu-hong. Vacuum Sealing Drainage [M]. Version 2. Beijing: People's Medical Publishing House, 2008: 3-34
- [11] Nugent N, Lannon D, O'Donnell M. Vacuum assisted closure a management option for the burns patient with exposed bone [J]. Burns, 2005, 31(3): 390-393
- [12] DeFranzo A J, Argenta LC, Mark sMW, et al. The use of vacuum-assisted closure therapy for the treatment of lower extremity wounds with exposed bone[J]. Plast Reconstr Surg, 2001, 108(5): 1184-1191
- [13] Clare MP, Fitzgibbons TC, McMullen ST, et al. Experience with the vacuum assisted closure negative pressure technique in the treatment of nonhealing diabetic and dysvascular wounds [J]. Foot Ankle Int, 2002, 23(10): 896-901
- [14] Huang WS, Hsieh SC, Hsieh CS, et al. Use of vacuum-assisted wound closure to manage limb wounds in patients suffering from acute necrotizing fasciitis[J]. Asian J Surg, 2006, 29(3): 135-139
- [15] Siegel IH J, Long JL, Watson KM, et al. Vacuum-assisted closure for Radiation associated wound complications [J]. J Surg Oncol, 2007, 96(7): 575-582

Hao Hu 等<sup>[9]</sup>研究发现,包括 miR-335 在内的 4 个 miRNAs 骨肉瘤 MG63 细胞系中低表达,这些异常表达的 miRNAs 可能在以后对骨肉瘤患者的诊疗和预后起到一定指示作用,但 miR-335 的低表达在骨肉瘤细胞生物学行为中所起到的作用未有进一步研究。本实验采取外源性转染 miR-335 模拟物促进骨肉瘤细胞内 miR-335 的表达,为了验证其在骨肉瘤细胞增殖、迁移和侵袭等生物学行为中起到的作用,分别进行了 MTT 和 Transwell 实验。MTT 比色结果显示实验组在转染 miR-335 后其细胞增殖能力较对照组明显降低。Transwell 迁移和侵袭实验也提示实验组细胞的迁移及侵袭能力较对照组明显降低。

本实验通过外源性转染 miR-335 模拟物提高骨肉瘤细胞系中 miR-335 的表达水平,证明了 miR-335 对体外培养的骨肉瘤细胞增殖和转移具有抑制作用,本实验为 miR-335 作为骨肉瘤诊治的新靶点提供了参考依据。

#### 参考文献(References)

- [1] Link MP. Osteosarcoma in adolescents and young adults: new developments and controversies. Commentary on the use of presurgical chemotherapy[J]. Cancer Treat Res, 1993, 62: 383-385
- [2] Jansson MD, Lund AH. MicroRNA and cancer[J]. Mol Oncol, 2012, 6: 590-610
- [3] Chen PS, Su JL, Hung MC. Dysregulation of microRNAs in cancer[J]. J Biomed Sci, 2012, 19: 90
- [4] Esquela-Kerscher A, Slack FJ. Oncomirs - microRNAs with a role in cancer[J]. Nat Rev Cancer, 2006, 6: 259-269
- [5] Hammond SM. MicroRNAs as tumor suppressors[J]. Nat Genet, 2007, 39: 582-583
- [6] Qin X, Yan L, Zhao X, et al. microRNA-21 overexpression contributes to cell proliferation by targeting PTEN in endometrioid endometrial cancer[J]. Oncol Lett, 2012, 4: 1290-1296
- [7] Rather MI, Nagashri MN, Swamy SS, et al. Oncogenic MicroRNA-155 Down-regulates Tumor Suppressor CDC73 and Promotes Oral Squamous Cell Carcinoma Cell Proliferation [J]. Implications For Cancer Therapeutics. J Biol Chem, 2013, 288: 608-618
- [8] Liu L, Yu X, Guo X, et al. miR-143 is downregulated in cervical cancer and promotes apoptosis and inhibits tumor formation by targeting Bcl-2[J]. Mol Med Report, 2012, 5: 753-760
- [9] Frampton AE, Krell J, Jacob J, et al. Loss of miR-126 is crucial to pancreatic cancer progression [J]. Expert Rev Anticancer Ther, 2012, 12: 881-884
- [10] Caldas C, Brenton JD. Sizing up miRNAs as cancer genes [J]. Nat Med, 2005, 11(7): 712-714
- [11] Calin GA, Croce CM. MicroRNA signatures in human cancers [J]. Nat Rev Cancer, 2006, 6(11): 857-866
- [12] Calin GA. Frequent deletions and down-regulation of microRNA genes miR15 and miR16 at 13q14 in chronic lymphocytic leukemia [J]. Proceedings of the National Academy of Sciences of the United States of America, 2002, 99(24): 15524-15529
- [13] Yubin Hao, Xinbin Gu, Yuan Zhao, et al. Enforced expression of miR-101 inhibits prostate cancer cell growth by modulating the COX-2 pathway in vivo cancer[J]. Med Oncol, 2011, 4(7): 1073-1083
- [14] XiangMin Li, AiMin Wang, Juan Zhang, et al. Down-regulation of miR-126 expression in colorectal cancer and its clinical significance [J]. Med Oncol, 2011, 28: 1054-1057
- [15] Zhenfeng Duan, Edwin Choy, David Harmon, et al. MicroRNA-199a-3p is downregulated in human osteosarcoma and regulates cell proliferation and migration[J]. Mol Cancer Ther, 2011, 10: 1337-1345
- [16] Heyn H, Engelmann M, Schreek S, et al. MicroRNA miR-335 is crucial for the BRCA1 regulatory cascade in breast cancer development[J]. Int J Cancer, 2011, (12): 2797-2806
- [17] Sorrentino A, Liu CG, Addario A, et al. Role of microRNAs in drug-resistant ovarian cancer cells[J]. Gynecol Oncol, 2008, (3): 478-486
- [18] Dohi O, Yasui K, Gen Y, et al. Epigenetic silencing of miR-335 and its host gene MEST in hepatocellular carcinoma[J]. J Oncol, 2013, (2): 411-418
- [19] Hu Hao, Zhang Yi, Cai Xian-hua, et al. Changes in microRNA expression in the MG-63 osteosarcoma cell line compared with osteoblasts[J]. Oncology Letters, 2012, (4): 1037-1042
- [16] KrberA, Frankson T, Grabbe S, et al. Vacuum assisted closure device improves the take of mesh grafts in chronic leg ulcer patients [J]. Dermatology, 2008, 216(3): 250-256
- [17] 吴彩玉, 王晓玲, 李艳容. 自行研发封闭式负压引流装置对难愈性伤口的治疗及护理[J]. 现代临床护理, 2011, 10(7): 31-33  
Wu Cai-yu, Wang Xiao-ling, Li Yan-rong. Developed its own treatment and care of closed suction drainage devices for refractory wounds treatment and nursing[J]. Modern Clinical Nursing, 2011, 10(7): 31-33
- [18] 陈立安, 陈健民, 黄炳生. 负压封闭引流术在慢性难愈合伤口治疗的应用[J]. 岭南现代临床外科, 2011, 11(6): 458-459  
Chen Li-an, Chen Jian-min, Huang Bing-sheng. Effect of vacuum sealing drainage on the treatment of chronic unhealed wounds[J]. Lingnan Modern Clinics in Surgery, 2011, 11(6): 458-459
- [19] 胡彩华, 黄春霞. 外用重组人表皮生长因子治疗烧伤创面的疗效观察[J]. 家庭护士, 2006, 4(10): 10  
Hu Cai-hua, Huang Chun-xia. Effect observation of For external use recombinant human epidermal growth factor on treating burn wound [J]. Family Nurse, 2006, 4(10): 10
- [20] 孙亚妮, 何娟. 金因肽与烧伤二号治疗压疮效果观察[J]. 中国美容医学, 2011, 20(9): 1379-1371  
Sun Ya-ni, He Juan. Observation of therapeutic effect of decubitus using Jin Yin Tai and NO. 2 Burning[J]. Chinese Journal of Aesthetic Medicine, 2011, 20(9): 1379-1371

(上接第 1314 页)