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液氮冷冻联合兰科肤宁治疗孕妇尖锐湿疣的临床效果评价*

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摘要 目的:评价液氮冷冻联合兰科肤宁治疗孕妇尖锐湿疣的临床疗效与安全性。**方法:**回顾性分析我院收治的46例患有尖锐湿疣的孕妇,平均年龄为27岁,妊娠平均18周。每例患者的病灶数为5~18个。应用液氮枪喷涂于皮损,液氮枪距皮损2-3 cm,喷雾时间60秒,重复操作直至喷嘴霜化。将蓝科肤宁喷涂于单层纱布,敷于皮损部位20分钟,每天2-3次,共1周。分别于治疗后1月、3月观察皮损愈合情况,评价治疗效果。**结果:**治疗5天后,皮损均治愈,所有患者除有轻度至中度疼痛外,无其他不适。治疗后1个月,满意度94%;治疗后3个月,满意度为87%。无色素脱失或瘢痕形成,无任何严重不良事件。每位孕妇均分娩出一个健康的婴儿,无分娩相关并发症。治疗后1个月,只有1例病人复发,复发率为2.2%。治疗后3个月,5例复发,复发率为10.9%。**结论:**液氮冷冻联合蓝科肤宁治疗孕妇尖锐湿疣的近期疗效较好,安全性较高。

关键词:尖锐湿疣;液氮冷冻;孕妇

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Evaluation of the Clinical Effect of Cryotherapy Combined with Lankefuning on the Pregnant Women with Condyloma Acuminata*

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ABSTRACT Objective: To evaluate the clinical effect and safety of cryotherapy combined with Lankefuning on the pregnant women with condyloma acuminata (CA). **Methods:** In this study, 46 cases of pregnant women with CA were treated with cryotherapy combined with Lankefuning. The mean age was 27 years (range, 23-34 years) and the patients were diagnosed with CA at a mean of 18 weeks (range, 10-26 weeks) gestation. The liquid nitrogen gun sprays liquid nitrogen to the lesions until the wart color changes from flesh colored to purple. The spray time was >60 sec and continued until the nozzle frosted (~2 min) and the nitrogen spray was no longer able to focus on the lesions. Then PC was sprayed on the non-woven fabric or single-layer gauze and applied to the affected area for 20 min, 2-3 times a day and for a period of one week. After three sessions, all patients were followed up for clinical evaluation at one months and three months. **Results:** The lesions were healed at 5 days after the treatment. All patients reported no discomfort, with the exception of mild to moderate pain. There was no visible warts after three sessions of cryotherapy and Lankefuning treatment. All patients were able to follow the treatment protocol, and responded to the survey with 94% satisfaction at 1 month and 87% satisfaction at 3 months after the completion of treatment. In one month' follow-up, only one case of recurrence was identified, and the recurrence rate was 2.2%. At three months, five cases of recurrence were identified, and the recurrence rate was 10.9%. No depigmentation or scar formation was observed, and no patients reported any severe adverse events. All pregnancies resulted in healthy live birth without delivery complications. **Conclusion:** Cryotherapy combined with Lankefuning was a safe and effective procedure for the treatment of pregnant women with CA.

Key words: Condyloma acuminata; Cryotherapy; Pregnancy

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引言

尖锐湿疣是人乳头瘤病毒(HPV)感染导致的生殖器皮损,孕妇患有尖锐湿疣的几率很高。妊娠期阴道分泌物明显增加,外阴处于潮湿、浸淫的状态,使得孕妇更容易患尖锐湿疣^[1,2]。与

妊娠有关的其他因素如妊娠激素水平变化、免疫功能降低等同样增加 HPV 感染的几率。孕妇患尖锐湿疣的特点为疣体增长速度快,患者的耐受性下降和依从性差^[3,4]。

孕妇尖锐湿疣的治疗方法主要包括双 / 三氯乙酸 (BCA/TCA)、冷冻疗法、电灼术、外科切除及激光治疗。这些治

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疗复发率较高,并且可能存在明显的副作用,包括局部溃疡和瘢痕形成,降低患者的依从性^[5,6]。此外,药物可能会造成胎儿畸形、激光治疗和手术切除对于耐受性较差的患者可能导致子宫收缩,甚至流产^[4,7]。冷冻疗法已广泛用于治疗CA。在冷冻治疗的过程中,液氮冻结疣体组织,从而导致疣体坏死。此外冷冻治疗还能刺激特定的免疫反应,如T淋巴细胞的免疫调节作用于残余的疣体组织^[8-10]。冷冻疗法的优点在于简单、便宜、很少导致疤痕或褪色,安全性高。

从银杏叶、莲花和其他植物中提取的原花青素是一种植物多酚,具有较强的抗氧化作用。研究显示原花青素具有抗菌、抗过敏和抗毒效果,抑制血小板聚集和降低毛细血管通透性^[11-13]。研究表明原花青素可以安全用于治疗婴儿、孕妇和老人的颜面部、会阴部和乳房等部位^[14,15]。同时,原花青素可以有效对抗红肿、渗出、瘙痒等炎症相关症状^[16,17]。因此,本研究应用液氮冷冻联合兰科肤宁(主要成份为原花青素)治疗孕妇尖锐湿疣,旨在评价其安全性和有效性。

1 资料与方法

1.1 临床资料

本研究回顾性研究分析了46名患有尖锐湿疣的孕妇患者,均通过液氮冷冻联合兰科肤宁进行治疗。病例来自于2010年5月至2013年2月西北妇女儿童医院(原陕西省妇幼保健院)皮肤科。患者平均年龄为27岁(23-34岁),妊娠平均18周(10-26周)。通过醋酸白试验^[18]、组织活检确诊尖锐湿疣。已告知患者液氮冷冻联合兰科肤宁治疗的优点,并明确告知患者可能出现流产、长期不孕以及其他相关的风险。本研究经由西北妇女儿童医院伦理委员会批准,所有患者都签署了知情同意书。

1.2 皮损特点

每例患者的病灶数为5~18个,平均每名患者 12.2 ± 5.5 个。疣的大小不同,但每个皮损都有一个宽蒂,具有清晰的边界,表面光滑、潮湿。在某些病人存在皮损融合。大多数病变呈灰褐色,少数呈暗红色。有12例皮损直径4cm。14例患者首次治疗,其余病例接受过2-10个月冷冻、激光治疗、电灼术和/或其他治疗包括手术、干扰素,5%咪喹莫特乳膏。4例患者有明显瘢痕形成。有流产的风险的患者被排除在研究之外。

1.3 皮损的治疗

首先将0.02%爱尔碘涂于皮损的表面,然后应用HX17 YDQ 500液氮枪(远西方科技有限公司北京,中国)喷涂于皮损。液氮枪距皮损2-3cm,喷雾时间60秒,重复操作直至喷嘴霜化(~2分钟),液氮不能聚焦于皮损。如果病人感觉疼痛,终止喷雾。如疼痛减轻,皮损再次喷雾直至皮损颜色由肉色变为紫色。将兰科肤宁(主要活性成分是原花青素,蓝科恒业医疗科技有限公司,中国长春)喷涂于单层纱布,敷于皮损部位20分钟,每天2-3次,共1周。

病人离开科室前,医生证实患者能通过手持镜子可以看到皮损。告知患者每天检查治疗区域,密切观察任何感染的症状,包括局部发红、肿胀、流液,或其他任何感染的迹象,包括发烧,应立即报告给医生。大多数病例治疗后3天后疣坏死组织开始脱落,1周后疣体完全脱落。疣体没有脱落的患者,疣体有不同程度缩小,并使用上述方法进行重复治疗。疣体消失,停止治疗。

1.4 病人随访

患者治疗前及每次复查均行拍照,治疗后1月、3月随访进行临床评价,包括检查病变复发、结垢、结痂脱离、形成疤痕、皮肤色素沉着及对疼痛的耐受情况。每次随访,调查病人对治疗的满意度(分为"非常满意","比较满意"或"不满意",以"非常满意","比较满意"计算满意度)。

2 结果

治疗5天后,皮损均治愈,所有患者除有轻度至中度疼痛外,无其他不适,治疗后无疣体可见。所有患者均能够按照要求进行随访,治疗后1月满意度94%,3个月满意度为87%。在某些患者,治疗区周围出现不同程度的水肿和红斑,伴有轻度至中度的灼热疼痛,但患者均能够忍受这些症状,顺利完成治疗。

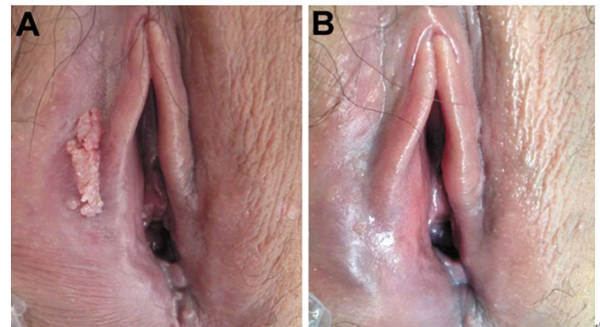


图1 病例1患者皮损。A:治疗前;B:液氮冷冻联合兰科肤宁治疗3次后。
Fig.1 Lesions of case 1. (A) Prior to treatment and (B) after cryotherapy and treatment with Lankefuning.

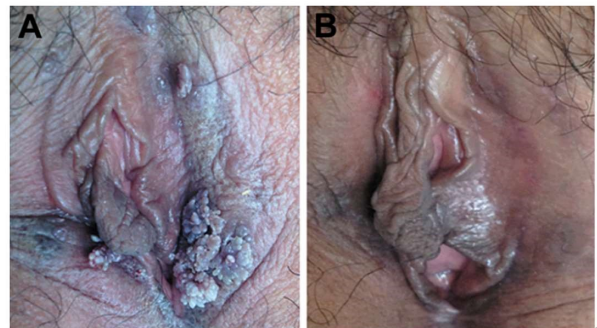


图2 病例2患者皮损。A:治疗前;B:液氮冷冻联合兰科肤宁治疗3次后。
Fig.2 Lesions of case 2. (A) Prior to treatment and (B) after cryotherapy and treatment with Lankefuning.

4例患者治疗后水泡破裂。兰科肤宁治疗后4天,损伤的组织均愈合。这些情况并没有影响后续的治疗。没有发现色素脱失或瘢痕形成,无任何严重不良事件。每一位孕妇均分娩出一个健康的婴儿,无分娩相关并发症。2例病人的治疗效果照片见图1与2。治疗后1个月,只有1例病人复发,复发率为2.2%。治疗后3月,5例复发,复发率为10.9%。结果见表1。

3 讨论

孕妇尖锐湿疣的特点是与非孕期比较,孕妇疣体的增长速度快,对治疗的不良反应严重。这可能是因为在怀孕期间免疫

表 1 孕妇尖锐湿疣的临床特点

Table I Clinical characteristics of pregnant women with CA.

Clinical characteristics	Number of patient (%)
Delivery mode	
Natural childbirth	19 (41.3)
Cesarean section	27 (58.7)
Birth weight (g)	
<2,500	1 (2.2)
2,500-4,000	41 (89.1)
>4,000	4 (8.7)
Gestational age (weeks)	
<36	4(8.7)
37-41	39 (84.8)
>42	3 (6.5)
Case of recurrence	
1 month	1 (2.2)
3 month	5 (10.9)

力降低,激素水平的变化(如:孕激素水平升高),阴道分泌物增加,导致皮损处于一个更潮湿的环境^[19,20]。仅有少数方法可用来治疗孕妇尖锐湿疣,包括有双 / 三氯乙酸(BCA/TCA)、冷冻疗法、电灼术、外科切除及激光治疗。咪喹莫特是一种免疫调节剂,可以导致轻度到重度红斑、局部糜烂、瘙痒和烧灼感;此外,少见的并发症有红肿、硬结、结痂、疼痛和压痛^[10,21]。在临床试验中,5%咪喹莫特乳膏治疗尖锐湿疣,复发率为 13-19%^[22]。咪喹莫特治疗妊娠期尖锐湿疣的安全性目前尚不明确。孕妇尖锐湿疣治疗方法还包括局部治疗,例如水杨酸、斑蝥素、鬼臼毒素、5-氟尿嘧啶、博来霉素及其他免疫调节治疗(干扰素)、物理破坏(手术切除、冷冻治疗、激光治疗)与顺势疗法^[23-25]。冷冻可引起组织坏死和激发特异性免疫反应^[23],是一种简单、廉价的治疗,很少引起疤痕或色素脱失,并且对孕妇是安全的。

在本研究中,我们通过喷雾冷冻治疗孕妇尖锐湿疣。液氮喷雾时间和剂量容易控制,较长的冻结时间可以更彻底的去除疣体。在治疗过程中,液氮接触到正常的皮肤和粘膜,这并没有造成严重的损害,只发现轻微的肿胀和非常表浅的损伤。疣体在低温下出现坏死。此外,冷冻治疗可诱导抗原特异性免疫反应和细胞因子的释放^[24]。从银杏叶、莲花和其他植物中提取的原花青素是一种植物多酚,具有较强的抗氧化作用。研究表明原花青素能抑制核因子 κ B 的 DNA 结合活性,从而阻断炎症性细胞的通路发挥抗炎作用^[14,26,27]。在结构上,原花青素包括至少一个芳香环和一个羟基,这使其可以很容易地结合自由基形成共振稳定的苯氧基^[28]。原花青素已经被证实用于怀孕妇女是安全的,并对发红、肿胀、渗出、瘙痒等炎症症状有效。

Yang 等^[6]通过应用光动力联合 5-氨基乙酰丙酸治疗 4 例孕妇尖锐湿疣,经过 6-24 月随访,疣体清除率为 100%,无 1 例复发,主要副作用包括轻度糜烂、疼痛与局部肿胀。所有孕妇都生产出健康婴儿,无分娩并发症。该研究只包括有 4 例患者,病

例数偏少。Huo 等^[29]通过局部热疗的方法治疗 2 例孕妇尖锐湿疣,局部温度为 44℃,持续 30 分钟,连续治疗 3 天,1 周后再治疗 2 天,之后每周治疗 1 次直至疣体完全消失。疣体分别于治疗后 5 周与 7 周消失,随访 6 月后未见复发。他们认为局部热疗可能会成为一种治疗孕妇尖锐湿疣的方法,其病例数只有 2 例。本研究应用液氮冷冻联合蓝科肤宁治疗 46 例孕妇尖锐湿疣,治疗 5 天后皮损均治愈,所有患者除有轻度至中度疼痛外,无其他不适。治疗后 1 月和 3 月,复发率分别为 2.2%和 10.9%。所有患者中,均没有观察到溃疡或疤痕,每一位孕妇均分娩出一个健康的婴儿,无分娩相关并发症,进一步证实了这种联合治疗的安全性。此外,治疗后 3 个月患者满意率达到 87%。但本研究也存在一定的局限性:① 病例数只有 46 例,将来需要更多的病例数,才能得出更加有说服力的结论;② 治疗后随访 3 月,随访时间偏短,需要更长时间的观察其复发情况。

总之,本研究结果表明液氮冷冻联合蓝科肤宁治疗孕妇尖锐湿疣的近期疗效较好,复发率相对较低,安全性较高,对胎儿没有明显影响。

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(上接第 5653 页)

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