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•综述•

膨胀纹注射治疗的研究进展

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[摘要] 膨胀纹是好发于全身张力部位的萎缩性条纹, 会严重影响美观, 对患者的心理造成极大困扰。临床上治疗膨胀纹的常规方法较多, 如激光光电、微针射频等, 但起效慢, 治疗效果欠佳。近年来, 注射疗法在膨胀纹治疗中得到越来越广泛的应用, 逐渐成为治疗热点。膨胀纹注射疗法包括低分子玻尿酸联合氨基酸疗法、富血小板血浆疗法、间充质干细胞疗法、聚左旋乳酸、聚己内酯等胶原蛋白刺激剂的注射疗法等。本文对膨胀纹注射治疗的研究进展作一综述, 旨在分析注射治疗用于改善膨胀纹的疗效及安全性, 探讨联合治疗在提高疗效中的作用, 以期膨胀纹的临床治疗提供一定参考价值。

[关键词] 膨胀纹; 注射治疗; 聚左旋乳酸; 富血小板血浆; 间充质干细胞

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Research Progress of Injection Therapy for Striae Distensae

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[Abstract] Striae distensae are atrophic stripes that commonly occur in tension areas throughout the body. They can seriously affect the appearance and cause great psychological distress to patients. There are many conventional methods for treating striae distensae clinically, such as laser photoelectric therapy and microneedle radiofrequency, but they have gradual effects and unsatisfactory treatment effects. In recent years, injection therapy has been increasingly used in the treatment of striae distensae and has gradually become a research hotspot. Injection therapies for striae distensae include the combination of low molecular hyaluronic acid and amino acids, platelet-rich plasma therapy, mesenchymal stem cell therapy and injection therapies with collagen stimulants such as poly-L-lactic acid and polycaprolactone. This paper reviews the research progress of injection therapy for striae distensae, aiming to analyze the efficacy and safety of injection therapy in improving striae distensae and explore the effect of combination therapy in enhancing the efficacy, so as to provide some reference value for the clinical treatment of striae distensae.

[Key words] Striae distensae; Injection therapy; Poly-L-lactic acid; Platelet-rich plasma; Mesenchymal stem cells

膨胀纹 (striae distensae, SD) 是一种条纹状皮肤病损, 人群中患病率11%~88%, 常见于女性, 发生在孕期称妊娠纹 (striae gravidarum, SG), 也可出现在青春期生长、肥胖等生理状态以及库欣综合征、类固醇使用过量导致的病理条件下^[1]。SD通常对称分布在腰腹、大腿、乳房等皮肤拉伸区域, 早期临床表现为光滑或微凸起的红纹 (striae rubrae, SR), 晚期表现为萎缩、起皱和色

素减退的凹陷型白色条纹 (striae albae, SA)。组织学分析显示SD的表皮萎缩, 真皮网棘消失, 胶原纤维束无序^[2], 是否出现SD的主要差异在75~95 μm 的深度 (真皮表皮交界处和真皮区域)^[3]。SD虽然没有健康威胁, 但会严重影响皮肤美观, 可能导致患者产生自卑、焦虑等不良情绪, 影响心理健康。目前, 该病的发病机制仍未明确, 其逐渐受到皮肤科、整形科等领域的广泛关注。本文对SD

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的注射治疗材料及机制的研究进展作一综述，以期临床相关实践提供参考。

1 膨胀纹的发病机制

皮肤的物理拉伸与体内激素变化被认为是主要诱导机制，而成纤维细胞代谢异常也参与其中。

1.1 皮肤机械牵拉 皮肤在机械牵拉后真皮弹性纤维网被破坏，胶原束显著分离，新生的富含原弹性蛋白的原纤维和胶原原纤维紊乱，无法形成胶原束提供弹性和支撑从而导致皮肤萎缩^[4]。机械牵拉导致胶原束分离，细胞外基质（extracellular matrix, ECM）的成分缺乏或功能障碍阻碍了这一过程的修复，比如金属蛋白酶MMP-7的异常上调^[3]。

1.2 激素变化 皮质类固醇激素在体内增加后，皮肤中胶原蛋白原肽以及对应的成纤维细胞中的I型胶原mRNA表达下降，诱导SD发生。Leite LL等^[5]报道过1例患者在1年之内因服用大量地塞米松和泼尼松后出现腹部膨胀条纹且并发溃疡的病例。Youssef SES等^[6]的研究发现，SG患者皮损处雌激素（ER）表达下降，雄激素受体（AR）、糖皮质激素受体（GR）表达增加。机制上雌激素能够降低皮肤金属蛋白酶MMPs的活性^[7]，抑制其对弹性蛋白和胶原蛋白的过度降解，而雌激素水平会随着雌激素受体的表达降低而降低，从而导致皮肤变薄，失去弹性；而雄激素具有促炎活性，被阻断后创面愈合加速。

1.3 成纤维细胞 Dong X等^[8]研究发现，早期SG成纤维细胞内的 α -平滑肌肌动蛋白含量显著增加，因而具有更强的收缩力，通过靶向I型胶原蛋白，恢复成纤维细胞的代谢活性是一种有效的治疗手段。另有研究发现^[2]，来自SD的成纤维细胞促纤维化信号通路FAK-PI3-AKT活性增强，而抗纤维化信号通路AMPK下调。因此，成纤维细胞可能是SD成因的研究新方向。

1.4 其他 胶原酶-2也被称为MMP-8，能切割I型胶原蛋白，而I型胶原是ECM的主要结构成分。Ozturk P等^[9]发现，SG患者中血清胶原酶-2的水平显著升高，可能是由于成纤维细胞的代谢异常促进了血清胶原酶-2的分泌。此外，血清松弛素水平随着妊娠期的进展而下降，较低的血清松弛素水平可能通过降低结缔组织的弹性而导致SG的发生。

2 膨胀纹的治疗方案

SD的常规治疗方法以点阵激光、微针射频等

光电技术为主。尽管微针射频与点阵激光治疗SD的临床效果相比其他能量设备好^[10]，但仍会出现红斑、色沉等不良反应^[11]，SD注射疗法以其微创性和明显的疗效受到越来越多医生的关注。

2.1 透明质酸 透明质酸（hyaluronic acid, HA）是一种大分子糖胺聚糖，是ECM的重要组成部分，能提高皮肤水分，通过刺激成纤维细胞活性增加胶原与弹性纤维密度，重塑ECM，改善皮肤质地，且研究证实HA在SD中具有明显疗效^[12, 13]。实际应用中，壁内流体技术（intra-mural fluid technique, ImFT）通过真皮内精准微滴注射递送HA，Fasola E等^[14]采用ImFT技术注射低分子HA与6种氨基酸混合的动能素治疗SD，4次治疗后临床改善率为96.5%，明显改善率达20.7%。射流体积重塑（jet volumetric remodeling, JVR）技术通过高速喷射原理使HA在真皮内匀速扩散^[15]。有研究^[16]采用交联HA结合JVR技术治疗SD，术后其条纹的颜色、纹理和轮廓均有改善，红斑、疼痛等不良反应轻微。由此可见，ImFT与JVR技术在真皮内递送HA是治疗SD的一种安全有效的手段。

2.2 可生物降解的胶原蛋白刺激剂 可生物降解的胶原蛋白刺激剂是新一代真皮填充剂，可刺激皮肤组织产生新的胶原蛋白，已广泛应用在面部年轻化领域。

2.2.1 聚左旋乳酸和聚双旋乳酸 聚左旋乳酸（poly-L-lactic acid, PLLA）和聚双旋乳酸（poly-D, L-lactide, PDLA）是具有生物相容性和可降解性的聚合物，通过轻微的炎症反应促进成纤维细胞增殖来诱导胶原蛋白合成^[17]。PDLA微球表面的多孔结构，使其比PLLA微球的实心结构具有更明显的早期增容效果，而PLLA微球刺激胶原合成更显著，是PDLA的1.1倍^[18, 19]。Cunha M^[20]做了5例关于PLLA改善SD的研究，将稀释后的PLLA微球注射在真皮内，共3次治疗，每次间隔30 d，末次治疗后评估，26%~50%的临床改善有2例，51%~75%的临床改善有3例，均无结节产生，且纹区真皮厚度增加。Seo SB等^[21]采用激光诱导微射流技术将PDLA微球透皮递送至皮内治疗SG，共4例患者接受5~7次治疗，术后32周3例患者的SG外观显著改善，无结节反应发生。

2.2.2 羟基磷灰石钙 羟基磷灰石钙（calcium hydroxyapatite, CaHa）是一种无机矿物，作为胶原蛋白刺激剂通常以微球形式悬浮在羧甲基纤维素载体（CMC）或HA等聚合物中，可改善皱纹及组

织容积缺失^[22, 23]。CaHa通过刺激成纤维细胞,促进血管生成增加来诱导新的胶原蛋白、弹性纤维产生^[24]。Lim JTE^[25]联合聚焦超声(MFU)和CaHa治疗10例SD患者,患者在3个病灶深度(4.5 mm、3.0 mm、1.5 mm)接受MFU-V治疗,随后采用25 G顿针在条纹内填充3~6 ml CaHa注射液(与生理盐水1:1稀释),半年后随访,2例患者获得50%~75%的改善,8例获得25%~50%的改善,稀释后的CaHa和MFU-V联合治疗在胶原再生,真皮组织重塑方面有协同作用。

2.2.3 聚己内酯 聚己内酯(polycaprolactone, PCL)是一种生物可吸收聚合物,通常利用羧甲基纤维素(CMC)凝胶载体,刺激胶原蛋白新生,增加皮肤厚度^[26]。Kim JS^[27]对13例患者行PCL于真皮内注射,1年后超声检测皮肤厚度平均增加(21.31 ± 4.34)%,组织学证实PCL微球注射周边成纤维细胞、胶原纤维和弹性纤维显著增加,且疗效可持续长达4年。新型无微粒PCL制剂(DLMR01)溶于水,可均匀渗透真皮层,避免传统PCL微粒(25~50 μm)的堵针及结节问题。Hong JY等^[28]治疗1例SG患者,使用33 G细针在真皮内注射,3D相机评估显示术后即刻改善,4个月后SG凹陷明显变平,提示PCL在降解过程中持续诱导胶原再生,实现“先填充后丰盈”的双重作用。

2.3 间充质干细胞 间充质干细胞(mesenchymal stem cells, MSCs)是一类具有多向分化潜能的干细胞,能从骨髓、脂肪、脐带等组织中分离^[29]。MSCs能促进成纤维细胞增殖和迁移,刺激胶原蛋白新生,重塑ECM,并通过旁分泌释放外泌体,抑制炎症,调节免疫细胞功能,加速皮肤修复^[30, 31]。Behrangi E等^[32]对比了微针联合人华通胶间充质干细胞(WJ-MSCs:脐带中的一种凝胶状物质)皮内注射与单纯微针治疗的疗效,10例SD患者接受3次治疗后,联合治疗组在皮肤超声参数上显著改善(真皮厚度、密度等),鉴于样本量小、疗程不足等原因,两组生物学指标改善的差异无统计学意义,但为MSCs在SD治疗中的应用提供了新方向。

除了上述多种外源性注射材料可用于治疗SD,自体来源的注射材料在SD的治疗中更安全。目前,自体来源材料包括脂肪干细胞胶、富血小板血浆、自体微移植植物等。其中,间充质干细胞既可来源于异体也可来源于自体。

2.4 脂肪干细胞胶 脂肪干细胞胶(stromal vascular fraction-gel, Svf-gel)是脂肪组织经物理方法祛除油滴后浓缩所得,富含脂肪干细胞和ECM,能促进成纤维细胞增殖,刺激胶原蛋白新生^[33, 34]。Li M等^[35]做了36例关于Svf-gel治疗SG的临床疗效研究,采用脂肪枪注射凹陷条纹,每点注射0.1 ml,术后6个月随访31例患者满意度为90%,SG的凹陷深度、面积、颜色均有改善。SVF-gel的存活率较高,大部分患者只要填充1次即可,降低了因传统脂肪填充的低存活率而过渡矫正导致的术后肿胀、脂肪液化等不良反应^[36]。

2.5 富血小板血浆 富血小板血浆(platelet rich plasma, PRP)通过离心自体全血后获得,富含生长因子,可促进成纤维细胞的增殖和活性来诱导胶原蛋白新生,并且PRP的抗炎特性有助于减轻治疗引起的红肿、色沉等不良反应,促进组织修复^[37, 38]。Gaiml HD等^[39]研究发现,PRP单独治疗SD的效果优于0.05%维甲酸。Madegowda SB等^[40]做了一项SD自身对照研究,发现PRP联合点阵CO₂激光治疗组的显著改善率高于激光组(33.3% > 16.6%),证实PRP的联合治疗对SD的改善更显著。Abdel-Motaleb AA等^[41]也证实微针联合PRP治疗SD比单独微针具有更好的促胶原蛋白和弹性纤维增加效果。由此可见,PRP无论是单独治疗还是联合治疗均为改善SD的有效方法。

2.6 自体微移植植物 自体微移植植物(autologous micrografting, AM)是由患者健康组织(如头皮毛囊、皮肤真皮层等)经分离系统(Human Brain Wave srl, Turin, Italy)处理后获得,通常被制备成生理盐水悬液使用。AM中含大量活性祖细胞,其属于成体干细胞,能分化成成熟的细胞促进组织修复与再生,可通过调节炎症和再生过程来改善皮肤凹陷与萎缩质地,Giřão L等^[42]做的10例SG患者的自身对照研究,证实了AM在SG治疗中的显著效果,术后3个月评估AM治疗侧的皮肤微循环增加240.1%,皮肤弹性增加216.5%,皮肤厚度增加26%,SG外观改善明显优于1.5 mm深的微针治疗侧,为SG的治疗提供了新的研究方向。

3 总结

膨胀纹的治疗中注射疗法应用目前已较常见,近年来一些新的注射材料与技术不断涌现,且疗效确切。从生理机制上看,聚左旋乳酸、聚己内酯与羟基磷灰石钙通过持续刺激胶原再生实

现组织重塑；富血小板血浆则通过多重生长因子调控促进细胞外基质修复；间充质干细胞具备多向分化潜能和旁分泌调节优势。较多临床证据表明透明质酸、聚左旋乳酸、羟基磷灰石钙、富血小板血浆、间充质干细胞等材料均能有效改善纹路外观。注射治疗联合点阵CO₂激光、微针、聚焦超声等手段具有增加膨胀纹的治疗效果，同时ImFT、激光微射流技术等递送技术可提升注射精准度及舒适性。膨胀纹的注射治疗虽有一定进展，但个体化联合治疗仍是未来的主要发展方向，通过优化材料组合及联合手段，可进一步提高有效成分的递送效率，协同促进胶原再生。

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