

玫瑰痤疮的治疗方法研究进展

李小岳, 燕华玲

青海大学附属医院, 皮肤科, 青海 西宁

收稿日期: 2023年5月21日; 录用日期: 2023年6月14日; 发布日期: 2023年6月21日

摘要

玫瑰痤疮(Rosecea)是一种常见累及面中部的慢性复发性炎症性疾病, 目前, 由于发病机制和病理生理学尚不完全清楚, 并缺乏生物标记和确切的药物靶点, 导致该病的治疗成为临床医生所面临的重要挑战之一。本文将针对目前国内外玫瑰痤疮的研究及治疗进展进行综述, 为临床治疗玫瑰痤疮优化治疗方法提供参考。

关键词

玫瑰痤疮, 复发性炎症, 治疗方法

Research Progress in the Treatment of Rosacea

Xiaoyue Li, Hualing Yan

Department of Dermatology, Qinghai University Affiliated Hospital, Xining Qinghai

Received: May 21st, 2023; accepted: Jun. 14th, 2023; published: Jun. 21st, 2023

Abstract

Rosecea is a common chronic recurrent inflammatory disease affecting the midface. Currently, the treatment of rosecea has become one of the important challenges faced by clinicians due to the lack of fully understood pathogenesis and pathophysiology, and the lack of biomarkers and exact drug targets. This article will review the current research and treatment progress of rosette acne at home and abroad, and provide reference for clinical treatment of rosette acne optimization treatment methods.

Keywords

Rosacea, Recurrent Inflammation, Treatment Methods

Copyright © 2023 by author(s) and Hans Publishers Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

1. 引言

玫瑰痤疮(又称酒渣鼻),是常发生在面中部(主要包括鼻部、口周及面部隆突部位)的一种慢性复发性炎症性皮肤病[1][2],在印度和欧亚最为流行,据调查显示德国的发病率为2.2%,瑞典的发病率为10%,且三十岁及以上的人群患玫瑰痤疮的概率为1%~22% [3][4][5]。研究显示玫瑰痤疮在发病人群中还存在性别差异,主要表现为女性发病较早的现象,且女性的患病率远大于男性的特点[6]。依据患者面中部皮肤呈现出的潮红、弥漫性红斑、炎性丘疹或脓疱及毛细血管扩张4种原发损害,可以将玫瑰痤疮分为四种类型,分别为I型:红斑毛细血管扩张型;II型:丘疹脓疱型;III型:肥厚型(又称鼻赘型);IV型:眼型[7]。且继发性表现如瘙痒、灼烧或刺痛[8]等是玫瑰痤疮患者常见的症状。目前国内外临床学者对于玫瑰痤疮的治疗方法主要包括:系统治疗、外用药物治疗及光电治疗[9],因此本文将从以下几个方面进行阐述。

2. 系统治疗

2.1. 抗生素类药物

在玫瑰痤疮的治疗中研究学者经过大量实验验证和分析,证明了玫瑰痤疮是慢性且易复发类炎症性疾病的一种[10][11]。在临床中,抗生素是玫瑰痤疮丘疹脓疱的一线系统治疗[12],在治疗玫瑰痤疮患者过程中,四环素类抗生素,包括多西环素、米诺环素、阿奇霉素、克拉霉素等是常用的药物。近年来,随着抗生素类药物治疗玫瑰痤疮的临床研究不断深入,逐渐得出亚抗菌剂量的多西环素不仅可以抑制白细胞趋化和选择性抑制细胞免疫,还能下调炎症细胞因子TNF- α 、IL-1的含量,同时还可以抑制一氧化氮介导的血管扩张,从而起到减少红斑的作用[13],其能用于治疗所有严重的炎症性丘疹、脓疱、临床炎症性水肿和玫瑰痤疮的眼部特征。多西环素在使用时产生的不良反应是致少数患者出现恶心、呕吐、腹胀等不同程度的胃肠道反应,甚至还会使患者出现头晕、嗜睡等不适症状,而对使用多西环素可能产生副作用的患者可以使用阿奇霉素进行治疗,阿奇霉素同样具有杀菌和免疫调节的作用[14]。甲硝唑是一种抗厌氧菌类的药物,具有抗毛囊蠕形螨及抗炎的效果,可作为玫瑰痤疮的二线用药[15]。

2.2. 维A酸类药物

异维A酸具有抗基质金属蛋白酶及抑制炎症细胞因子的作用,可作为增生肥大型玫瑰痤疮患者的首选系统治疗药物,以及丘疹脓疱型患者在其他治疗效果不佳情况下的二线选择[16]。赵旭明等[17]研究表明,低剂量异维A酸可有效治疗难治性丘疹脓疱型玫瑰痤疮,改善患者生活质量,降低短期复发率。徐晓静等[18]认为不同剂量的异维A酸在玫瑰痤疮的治疗过程中有较好的临床疗效,安全性及患者满意度较高。对于顽固难治性丘疹脓疱型玫瑰痤疮还可选异维A酸胶囊,患者在使用异维A酸时会产生一定的负面影响,可能加重患者阵发性潮红症状,还可能导致肝功能和血脂异常等。

2.3. 羟氯喹

羟氯喹具有抗炎、抗免疫、抗紫外线损伤等多种功效, 有研究表明, 羟氯喹可通过抑制 LL-37 诱导激活的肥大细胞, 达到减少炎症因子释放的目的, 对于阵发性潮红或红斑的改善优于丘疹和脓疱[19]。羟氯喹还能够抑制抗原肽-MHC 蛋白物的形成, 减少对 CD4⁺细胞的刺激, 进而降低自身抗原肽的免疫反应, 其还能够一定程度的阻止炎症性细胞免疫因子的释放, 降低嗜酸性粒细胞的趋化性和中性粒细胞的吞噬作用, 从而发挥其免疫抑制及抗炎的作用[20], 对一些同时伴有明显红斑或毛细血管扩张的患者, 可以考虑抗微生物类药物(多西环素、甲硝唑等)联合羟氯喹治疗。有研究显示多西环素联合羟氯喹治疗玫瑰痤疮有效率高达 76.9%, 与单一羟氯喹治疗相比疗效更加显著, 证明了多西环素和羟氯喹联合使用时可提高玫瑰痤疮的治疗效果[21]。Guiguemde 等研究证明了约有 5%~10%的玫瑰痤疮患者口服羟氯喹后会出现轻微的不良反应, 如胃肠道反应及皮疹[22]。严重的眼毒性在一些少见的病例中也曾被报道, 故如果连续使用超过 3~6 个月, 建议行眼底检查, 以排除视网膜病变。

2.4. β 肾上腺素能受体抑制剂

通过对临床经验和病例报告的综合分析, ROSCO 小组认为治疗玫瑰痤疮时局部使用 α -肾上腺素和口服 β 受体阻滞剂也是一种可行的治疗方法, 特别是局部肾上腺素能类的布溴莫尼定和口服 β 受体阻滞剂类的卡维地洛[23]。卡维地洛本身具有 α_1 受体阻滞和非选择性 β 受体阻滞作用, 可作用于心肌 β_1 肾上腺素受体进而减慢心率, 起到减缓患者紧张情绪的作用, 主要对难治性阵发性潮红和持续性红斑明显的患者有明显的效果[24]。Pietschke 等[25]学者证明, 卡维地洛能长期有效地治疗面部红斑和持续性红斑, 且患者的满意度明显提高。Seo 等[26]对 24 例应用卡维地洛治疗面部红斑的患者进行回顾性分析, 所有患者均口服卡维地洛 6.25 mg, 每日一次或两次, 每日剂量逐渐增加至 12.5 mg, 通过临床红斑评定量表(CEA)评分和医生整体评价法(PSA)评分进行评估, 结果表明有明显改善。但在使用卡维地洛的过程中应时刻关注患者是否出现血压过低和心跳过缓的情况, 注意监测心率和血压。

3. 局部治疗

在玫瑰痤疮干预的研究中, 局部溴莫尼定和羟甲唑啉能够治疗暂时持续性红斑, 局部壬二酸、伊维菌素、甲硝唑和米诺环素推荐用于治疗丘疹、脓疱[27]。壬二酸是一种常用的抗菌药物, 能够有效的抑制痤疮内的细菌, 进一步减少皮肤表面分泌皮脂腺和脂肪酸。Coda 等[28]使用 15%的壬二酸凝胶治疗患者, 每日涂抹两次, 通过分析得出此方法能够明显抑制 SPA 的活性及降低玫瑰痤疮皮损中 KLK5 (激肽释放酶)水平的增加, 进而缓解患者的病情; 而 15%的壬二酸泡沫剂经过临床试验, 验证了比传统的凝胶剂治疗效果更好, 在使用中每日两次且连续使用 12 周以上效果会更加显著, 其中约 10.6%的使用者没有灼热、瘙痒或者刺痛等不良反应, 使用壬二酸凝胶会有高达 38%的患者产生不良反应[29]。

异维 A 酸红霉素凝胶是一种复合制剂, 由抗生素和维甲酸合制而成, 其抗炎及抑制皮脂分泌有明显的治疗效果[30]。在研究中局部异维菌素被证明是治疗丘疹性红斑痤疮最有效的局部治疗方法[31]。局部伊维菌素不仅能用于轻度丘疹性红斑痤疮或轻度红斑痤疮的皮肤区, 也适用于中度至重度红斑痤疮的患者[32]。

甲硝唑可作为凝胶或乳膏形式供患者使用, 是治疗玫瑰痤疮较为受欢迎的外用药物之一。0.75%甲硝唑凝胶[33]和 1%甲硝唑乳膏[34]、0.75%甲硝唑乳膏[35]和甲硝唑乳液[36]在临中经过实验分析, 证明了在 8~12 周内患者每天涂抹一到两次能够有效缓解玫瑰痤疮的症状, 在这些研究的结果中得出不论是凝胶还是乳膏都能显著抑制炎症病变, 能够减少与玫瑰痤疮产生相关的红斑, 此外, 面霜和凝胶似乎都对毛细血管扩张没有较明显的影响。

米诺环素泡沫是一种新型药物,首次使用时用于治疗中重度寻常痤疮[37],研究学者在两项随机临床试验中,分析并证实了米诺环素泡沫治疗中度至重度丘疹性红斑痤疮的疗效及安全性[38]。在一项前瞻性双盲研究中显示,3%的局部米诺环素凝胶对丘疹性红斑痤疮患者的治疗是有益的,与载体相比,炎症病变显著减少[39]。

4. 光电治疗

在玫瑰痤疮的治疗中,光电治疗是一种较新的治疗手段,在最新的系统综述中推荐使用激光和强脉冲光(intensive pulse light, IPL)疗法治疗红斑,尤其是毛细血管扩张[40]。Kim 等[41]人在利用光电治疗玫瑰痤疮的研究中发现当以相同的能量和脉冲使用时,短脉冲 ILP 治疗和脉冲染料激光治疗玫瑰痤疮在黑色素或红斑指数方面没有观察到显著差异。Liu 等[42]人研究发现, IPL 对持久性红斑影响甚微, IPL 可用于毛细血管扩张型与丘疹脓疱型玫瑰痤疮的临床治疗,尤其对于丘疹脓疱型玫瑰痤疮炎性皮损周边红斑疗效更佳。Zhang 等[43]人在对 807 名患有不同亚型玫瑰痤疮患者的回顾性研究中,其症状包括红斑、毛细血管扩张、丘疹、脓疱和鼻赘等不同类型的玫瑰痤疮均可以利用光电治疗,且指出多个连续的光、激光设备可用于治疗鼻型玫瑰痤疮。Friedmann 等[44]人证实了 Nd:YAG 激光对毛细血管扩张疗效更佳, PDL 更适合伴轻度毛细血管扩张的红斑。Lee 等[45]人使用 Nd:YAG 激光治疗顽固性毛细血管扩张症有较好效果,单次治疗后 12 周血管清除率达 78.3%,提示涵盖靶色基血红蛋白的 PDL、Nd:YAG 激光均可有效治疗玫瑰痤疮。

CO₂ 激光和 Er:YAG 可用于治疗玫瑰痤疮,其机制在于加热靶目标水分子,引起浅层皮肤快速升温,通过烧灼剥脱作用去除增生组织[46]。Er:YAG 相比 CO₂ 激光热效应低,其对患者造成炎症后色素沉着概率低,并降低治疗时的疼痛感[47]。Meesters 等[48]人采用 CO₂ 激光分次治疗鼻赘型玫瑰痤疮患者,结果显示皮脂分泌、瘙痒症状明显改善,表明 CO₂ 激光分次治疗可有效治疗轻度鼻赘型玫瑰痤疮,且较外科手术副作用更少、误工期更短。Orenstein 等人利用 Er:YAG 激光对 6 例鼻赘型患者进行治疗,单次治疗后在 1~2 年间根据患者反映,对其治疗结果均满意,且未出现并发症[49]。

近年有对激光和光疗以及其他方法的联合治疗方案进行了研究, Tanghetti 等[50]人针对 46 名患者的 4 期、多中心、介入性、开放标签的研究结果表明,羟甲唑啉能够作为能量疗法的辅助药物,可用于治疗玫瑰痤疮中度至重度持续性面部红斑症状。Suggs 等[51]人对 31 名受试者的研究结果显示,脉冲染料激光和 1.0%羟甲唑啉乳膏组合治疗方法能够安全有效地减少了红斑和毛细血管扩张。

5. 手术治疗

对于玫瑰痤疮患者有较严重的鼻赘增生时可以考虑手术切除治疗,去除增生组织,使其面部组织形状大致恢复正常[52]。在鼻赘较严重的情况下临床医生在进行手术切除的同时还应对照患者在正常情况下的面部状况,尽量达到手术切除组织量适中,避免切除过多或不足,在进行手术过程中由于面部血管密集,可能会导致出血过多的情况。

6. 总结与展望

截止目前还没有单一的且疗效较好的药物能够治疗不同症状的玫瑰痤疮,且有些药物在患者使用以后会有一些副作用,影响患者的健康。临床治疗玫瑰痤疮的主要方法是系统用药、局部外用药物、光电治疗等方法,联合治疗的方法是当前治疗玫瑰痤疮较为前沿的手段。玫瑰痤疮是易复发、难根治的慢性炎症疾病,在治疗中还应考虑该病的病因、病理机制、药物对患者健康等因素的影响,为治疗玫瑰痤疮提供更加明显可靠的方法。

参考文献

- [1] Wollina, U. (2019) Is Rosacea a Systemic Disease? *Clinics in Dermatology*, **37**, 629-635. <https://doi.org/10.1016/j.clindermatol.2019.07.032>
- [2] Ahn, C.S. and Huang, W.W. (2018) Rosacea Pathogenesis. *Dermatologic Clinics*, **36**, 81-86. <https://doi.org/10.1016/j.det.2017.11.001>
- [3] Wollina, U. (2014) Recent Advances in the Understanding and Management of Rosacea. *F1000 Medicine Reports*, **6**, 50. <https://doi.org/10.12703/P6-50>
- [4] Berg, M. and Liden, S. (1989) An Epidemiological Study of Rosacea. *Acta Dermato-Venereologica*, **69**, 419-423.
- [5] Parisi, R. and Yiu, Z.Z.N. (2018) The Worldwide Epidemiology of Rosacea. *British Journal of Dermatology*, **179**, 239-240.
- [6] Wang, Y., Zhao, Z., Liu, F., et al. (2020) Relationship between the Incidence of Rosacea and Drinking or Smoking in China. *Journal of Central South University. Medical Sciences*, **45**, 165-168.
- [7] Gallo, R.L., Granstein, R.D., Kang, S., Mannis, M., Steinhoff, M., Tan, J. and Thiboutot, D. (2018) Standard Classification and Pathophysiology of Rosacea: The 2017 Update by the National Rosacea Society Expert Committee. *Journal of the American Academy of Dermatology*, **78**, 148-155. <https://doi.org/10.1016/j.jaad.2017.08.037>
- [8] Johnson, S.M., Berg, A. and Barr, C. (2020) Managing Rosacea in the Clinic: From Pathophysiology to Treatment—A Review of the Literature. *The Journal of Clinical and Aesthetic Dermatology*, **13**, S17-S22.
- [9] Wilkin, J., Dahl, M., Detmar, M., et al. (2004) Standard Grading System for Rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea. *Journal of the American Academy of Dermatology*, **50**, 907-912. <https://doi.org/10.1016/j.jaad.2004.01.048>
- [10] Rosso, J.D. (2012) Advances in Understanding and Managing Rosacea: Part 1: Connecting the Dots between Pathophysiological Mechanisms and Common Clinical Features of Rosacea with Emphasis on Vascular Changes and Facial Erythema. *Journal of Clinical & Aesthetic Dermatology*, **5**, 16-25.
- [11] Two, A.M. and Del Rosso, J.Q. (2014) Kallikrein 5-Mediated Inflammation in Rosacea: Clinically Relevant Correlations with Acute and Chronic Manifestations in Rosacea and How Individual Treatments May Provide Therapeutic Benefit. *Journal of Clinical & Aesthetic Dermatology*, **7**, 20-25.
- [12] 潘廷猛, 陈雪路, 施雯, 荣光辉, 何彩凤. 羟氯喹联合多西环素序贯光电协同治疗 I 型及 II 型玫瑰痤疮临床观察[J]. 中国美容医学, 2020, 29(9): 22-26.
- [13] Schaller, M., Almeida, L., Bewley, A., et al. (2017) Rosacea Treatment Update: Recommendations from the Global ROSacea COnsensus (ROSCO) Panel. *British Journal of Dermatology*, **176**, 465-471. <https://doi.org/10.1111/bjd.15173>
- [14] Kim, J.H., Oh, Y.S. and Choi, E.H. (2011) Oral Azithromycin for Treatment of Intractable Rosacea. *Journal of Korean Medical Science*, **26**, 694-696. <https://doi.org/10.3346/jkms.2011.26.5.694>
- [15] Rezaković, S., Mokos, Z.B. and Paštar, Z. (2015) Pyridoxine Induced Rosacea-Like Dermatitis. *Acta Clinica Croatica*, **54**, 99-102.
- [16] Lee, G.L. and Zirwas, M.J. (2015) Granulomatous Rosacea and Periorificial Dermatitis. *Dermatologic Clinics*, **33**, 447-455. <https://doi.org/10.1016/j.det.2015.03.009>
- [17] 赵旭明, 温杰, 吴远慧, 等. 低剂量异维 A 酸治疗难治性丘疹脓疱型玫瑰痤疮的临床疗效[J]. 中国中西医结合皮肤性病学杂志, 2021, 20(6): 557-560.
- [18] 徐晓静, 朱元杰. 不同剂量异维 A 酸联合脉冲染料激光治疗酒渣鼻的疗效及安全性分析[J]. 中国美容医学, 2021, 30(1): 73-76.
- [19] Wang, B., Yuan, X., Huang, X., et al. (2021) Efficacy and Safety of Hydroxychloroquine for Treatment of Patients with Rosacea: A Multicenter, Randomized, Double-Blind, Double-Dummy, Pilot Study. *Journal of the American Academy of Dermatology*, **84**, 543-545. <https://doi.org/10.1016/j.jaad.2020.05.050>
- [20] Schaller, M., Almeida, L.M., Bewley, A., Cribier, B., et al. (2017) Rosacea Treatment Update: Recommendations from the Global ROSacea COnsensus (ROSCO) Panel. *British Journal of Dermatology*, **176**, 465-471. <https://doi.org/10.1111/bjd.15173>
- [21] 刘乐, 陈文慧. 羟氯喹联合盐酸多西环素治疗玫瑰痤疮疗效观察[J]. 中国中西医结合皮肤性病学杂志, 2020, 19(5): 431-432.
- [22] Guiguemde, W., Shelat, A., Garcia-Bustos, J., et al. (2012) Global Phenotypic Screening for Antimalarials. *Chemistry & Biology*, **19**, 116-129. <https://doi.org/10.1016/j.chembiol.2012.01.004>
- [23] Schaller, M., Almeida, L.M.C., Bewley, A., Cribier, B., et al. (2020) Recommendations for Rosacea Diagnosis, Classi-

- fication and Management: Update from the Global Rosacea Consensus 2019 Panel. *British Journal of Dermatology*, **182**, 1269-1276. <https://doi.org/10.1111/bjd.18420>
- [24] Hsu, C.C. and Lee, J.Y. (2011) Carvedilol for the Treatment of Refractory Facial Flushing and Persistent Erythema of Rosacea. *Archives of Dermatology*, **147**, 1258-1260. <https://doi.org/10.1001/archdermatol.2011.204>
- [25] Pietschke, K. and Schaller, M. (2017) Long-Term Management of Distinct Facial Flushing and Persistent Erythema of Rosacea by Treatment with Carvedilol. *Journal of Dermatological Treatment*, **29**, 310-313. <https://doi.org/10.1080/09546634.2017.1360991>
- [26] Seo, B.H., Dong, H.K., Suh, H.S., *et al.* (2020) Facial Flushing and Erythema of Rosacea Improved by Carvedilol. *Dermatologic Therapy*, **33**, e14520.
- [27] van Zuuren, E.J., Fedorowicz, Z., Tan, J., van der Linden, M.M.D., Arents, B.W.M., Carter, B. and Charland, L. (2019) Interventions for Rosacea Based on the Phenotype Approach: An Updated Systematic Review Including GRADE Assessments. *British Journal of Dermatology*, **181**, 65-79. <https://doi.org/10.1111/bjd.17590>
- [28] Coda, A.B., Hata, T., Miller, J., *et al.* (2013) Cathelicidin, Kallikrein 5, and Serine Protease Activity Is Inhibited during Treatment of Rosacea with Azelaic Acid 15% Gel. *Journal of the American Academy of Dermatology*, **69**, 570-577. <https://doi.org/10.1016/j.jaad.2013.05.019>
- [29] Nakagawa, H., Nemoto, O., Igarashi, A., Saeki, H., Kabashima, K., Oda, M. and Nagata, T. (2021) Delgocitinib Ointment in Pediatric Patients with Atopic Dermatitis: A Phase 3, Randomized, Double-Blind, Vehicle-Controlled Study and a Subsequent Open-Label, Long-Term Study. *Journal of the American Academy of Dermatology*, **85**, 854-862. <https://doi.org/10.1016/j.jaad.2021.06.014>
- [30] Starosta, D.A. and Lorenz, B. (2021) Pediatric Ocular Rosacea Effectively Treated with Topical 1.5% Azithromycin Eye Drops. *Der Ophthalmologe*, **118**, 68-73. <https://doi.org/10.1007/s00347-020-01279-z>
- [31] Husein-El Ahmed, H. and Steinhoff, M. (2020) Efficacy of Topical Ivermectin and Impact on Quality of Life in Patients with Papulopustular Rosacea: A Systematic Review and Meta-Analysis. *Dermatologic Therapy*, **33**, e13203. <https://doi.org/10.1111/dth.13203>
- [32] Trave, I., Merlo, G., Cozzani, E., *et al.* (2019) Real-Life Experience on Effectiveness and Tolerability of Topical Ivermectin in Papulopustular Rosacea and Antiparasitic Effect on Demodex Mites. *Dermatologic Therapy*, **32**, e13093. <https://doi.org/10.1111/dth.13093>
- [33] Aronson, I.K., Rumsfield, J.A., West, D.P., *et al.* (1987) Evaluation of Topical Metronidazole Gel in Acne Rosacea. *Drug Intelligence & Clinical Pharmacy*, **21**, 346-351. <https://doi.org/10.1177/106002808702100410>
- [34] Nielsen, P.G. (1983) Treatment of Rosacea with 1% Metronidazole Cream. A Double-Blind Study. *British Journal of Dermatology*, **108**, 327-332. <https://doi.org/10.1111/j.1365-2133.1983.tb03972.x>
- [35] Maddin, S. (1999) A Comparison of Topical Azelaic Acid 20% Cream and Topical Metronidazole 0.75% Cream in the Treatment of Patients with Papulopustular Rosacea. *Journal of the American Academy of Dermatology*, **40**, 961-965. [https://doi.org/10.1016/S0190-9622\(99\)70085-X](https://doi.org/10.1016/S0190-9622(99)70085-X)
- [36] Elewski, B.E., Fleischer, A.B. and Pariser, D.M. (2019) A Comparison of 15% Azelaic Acid Gel and 0.75% Metronidazole Gel in the Topical Treatment of Papulopustular Rosacea Results of a Randomized Trial. <https://doi.org/10.1001/archderm.139.11.1444>
- [37] Shemer, A., Shiri, J., Mashiah, J., *et al.* (2016) Topical Minocycline Foam for Moderate to Severe Acne Vulgaris: Phase 2 Randomized Double-Blind, Vehicle-Controlled Study Results. *Journal of the American Academy of Dermatology*, **74**, 1251-1252. <https://doi.org/10.1016/j.jaad.2015.09.065>
- [38] Gold, L.S., Del Rosso, J.Q., Kircik, L., *et al.* (2020) Minocycline 1.5% Foam for the Topical Treatment of Moderate to Severe Papulopustular Rosacea: Results of 2 Phase 3, Randomized, Clinical Trials. *Journal of the American Academy of Dermatology*, **82**, 1166-1173. <https://doi.org/10.1016/j.jaad.2020.01.043>
- [39] Webster, G., Draelos, Z.D., Graber, E., *et al.* (2020) A Multicentre, Randomized, Double-Masked, Parallel Group, Vehicle-Controlled Phase IIb Study to Evaluate the Safety and Efficacy of 1% and 3% Topical Minocycline Gel in Patients with Papulopustular Rosacea. *British Journal of Dermatology*, **183**, 471-479. <https://doi.org/10.1111/bjd.18857>
- [40] Zuuren, E.J.V., Fedorowicz, Z., Tan, J., *et al.* (2019) Evidence-Based Treatments for Rosacea Based on Phenotype Approach. *British Journal of Dermatology*, **181**, e16. <https://doi.org/10.1111/bjd.18064>
- [41] Kim, B.Y., Moon, H.R. and Ryu, H.J. (2019) Comparative Efficacy of Short-Pulsed Intense Pulsed Light and Pulsed Dye Laser to Treat Rosacea. *Journal of Cosmetic and Laser Therapy*, **21**, 291-296. <https://doi.org/10.1080/14764172.2018.1528371>
- [42] Liu, J., Liu, J., Ren, Y., *et al.* (2014) Comparative Efficacy of Intense Pulsed Light for Different Erythema Associated with Rosacea. *Journal of Cosmetic and Laser Therapy*, **16**, 324-327. <https://doi.org/10.3109/14764172.2014.957218>
- [43] Zhang, Y., Jiang, S., Lu, Y., *et al.* (2020) A Decade Retrospective Study of Light/Laser Devices in Treating Nasal Ro-

- sacea. *Journal of Dermatological Treatment*, **31**, 84-90. <https://doi.org/10.1080/09546634.2019.1580669>
- [44] Friedmann, D.P., Goldman, M.P., Fabi, S.G., *et al.* (2018) Comparison of Efficacy between Long-Pulsed Nd:YAG Laser and Pulsed Dye Laser to Treat Rosacea-Associated Nasal Telangiectasia. *Journal of Cosmetic and Laser Therapy*, **20**, 260-264. <https://doi.org/10.1080/14764172.2017.1418510>
- [45] Lee, J.H., Na, S.Y., Choi, M., *et al.* (2012) Long-Pulsed Nd:YAG Laser: Does It Give Clinical Benefit on the Treatment of Resistant Telangiectasia? *The Journal of the European Academy of Dermatology and Venereology*, **26**, 1280-1284. <https://doi.org/10.1111/j.1468-3083.2011.04282.x>
- [46] 中国医师协会皮肤科医师分会皮肤美容亚专业委员会. 中国玫瑰痤疮诊疗专家共识(2016) [J]. 中华皮肤科杂志, 2017, 50(3): 156-157.
- [47] 赵梓刚, 李承新. 玫瑰痤疮的非药物治疗[J]. 皮肤病与性病, 2017, 40(2): 96-98.
- [48] Meesters, A.A., van der Linden, M.M. and De Rie, M.A. (2015) Fractionated Carbon Dioxide Laser Therapy as Treatment of Mild Rhinophyma: Report of Three Cases. *Dermatologic Therapy* **28**, 147-150. <https://doi.org/10.1111/dth.12205>
- [49] Orenstein, A., Haik, J., Tamir, J., *et al.* (2001) Treatment of Rhinophyma with Er:YAG Laser. *Lasers in Surgery and Medicine*, **29**, 230-235. <https://doi.org/10.1002/lsm.1112>
- [50] Tanghetti, E.A., Goldberg, D.J., Dover, J.S., Geronemus, R.G., Bai, Z., Alvandi, N. and Shanler, S.D. (2021) Oxymetazoline and Energy-Based Therapy in Patients with Rosacea: Evaluation of the Safety and Tolerability in an Open-Label, Interventional Study. *Lasers in Surgery and Medicine*, **53**, 55-65. <https://doi.org/10.1002/lsm.23253>
- [51] Suggs, A.K., Macri, A., Richmond, H., Munavalli, G. and Friedman, P.M. (2020) Treatment of Erythematotelangiectatic Rosacea with Pulsed-Dye Laser and Oxymetazoline 1.0% Cream: A Retrospective Study. *Lasers in Surgery and Medicine*, **52**, 38-43. <https://doi.org/10.1002/lsm.23176>
- [52] 方方, 张国成. 协和皮肤外科学[M]. 北京: 中国协和医科大学出版社, 2008: 124-125.