

头皮脂溢性皮炎外用药物治疗的研究进展

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摘要

脂溢性皮炎是皮肤科常见的慢性炎症性皮肤病, 好发于头面、躯干等皮脂腺丰富区。致病机制尚未完全明确, 其临床表现多样, 治疗方式多种。局部外用药物治疗因为效果良好、操作便捷、系统不良反应少等优点, 更多地用于头皮脂溢性皮炎的治疗。本文就头皮脂溢性皮炎的外用药物治疗进行综述。

关键词

头皮脂溢性皮炎, 外用药物, 治疗

Research Progress of Topical Medication Treatment for Seborrheic Dermatitis of Scalp

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Abstract

Seborrheic dermatitis is a common chronic inflammatory skin disease in dermatology, which occurs in sebaceous gland-rich areas such as head, face and trunk. The pathogenic mechanism is not completely clear, and its clinical manifestations and treatment methods are diverse. Topical drug therapy is more used to treat seborrheic dermatitis of scalp because of its good effect, convenient

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operation and less systemic adverse reactions. This paper reviews the topical drug treatment of seborrheic dermatitis of scalp.

Keywords

Seborrheic Dermatitis of Scalp, Topical Medicine, Treat

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1. 引言

脂溢性皮炎(Seborrheic Dermatitis, SD)系发生在皮脂溢出部位的一种慢性丘疹鳞屑性、浅表炎症性皮肤病[1],这种疾病在男性中比女性更常见,在婴儿期和青春期后的任何年龄都可能发生[2]。好发于头面、躯干等皮脂腺丰富区。头部的轻型损害为小片灰白色糠秕状或油腻性鳞屑性斑片,基底潮红。以后逐渐扩展,融合成边界清楚的地图状大斑片,严重者累及大部分头部,覆有油腻性厚痂,可有渗出,伴有腥臭味[1]。

头皮脂溢性皮炎很普遍,表现为一种慢性炎症性皮肤病,随着时间的推移往往会复发。虽然这是一种相当常见的疾病,但其发病机制仍然尚未完全明确[3]。可能与真菌感染(特别是马拉色菌属)、脂质代谢、免疫因素、遗传因素、皮肤屏障受损等有关[4]。头皮脂溢性皮炎的治疗主要有系统治疗(B族维生素、抗生素、抗真菌药物、糖皮质激素等)及局部治疗(角质溶解剂、抗真菌药物、抗炎药物等)。局部外用药物治疗因为效果良好、操作便捷、系统不良反应少等优点,更多地用于头皮脂溢性皮炎的治疗。下面介绍主要用于治疗头皮脂溢性皮炎的外用药物。

2. 角质溶解剂

2.1. 煤焦油

煤焦油是制备焦炭过程中的副产品。煤焦油同时具有工业和医疗用途,通常,煤焦油在配方中(含0.5%~3%)用作抗增殖和消炎剂,可使皮肤角质蛋白变得更柔软,并减缓皮肤细胞的生长速度。Nenoff等通过琼脂稀释技术测定受试药物的最低抑菌浓度(MIC),发现煤焦油凝胶能够在体外抑制54种糠秕马拉色菌分离株中的52种生长,MIC值在625至10,000 $\mu\text{g/mL}$ 之间,表明煤焦油凝胶软膏在体内治疗头皮屑和脂溢性皮炎中的效果可能至少部分归因于煤焦油的抗真菌活性以及凝胶基质的抗真菌活性[5]。Claudine Piérard-Franchimont等人对30名受试者进行了临床评估和受试者自我评估,0.5%煤焦油洗发水在治疗第1周就可以有效缓解头皮屑和瘙痒的症状[6]。

2.2. 水杨酸

水杨酸可减少角质细胞之间的粘附,从而去除角化过度的皮肤。0.5%~2%之间(甚至5%)的糊剂和软膏中,有角质形成作用。5%~20%的浓度时对角质层有迅速的角质层松解作用[1]。水杨酸同时具有微弱的杀菌和抗菌作用[7]。胡杏林等人以受试者自身治疗前后为对照,外用水杨酸去屑护发露,每日或隔日1次。发现含有水杨酸的去屑护发露可以有效地改善脂溢性皮炎的头皮瘙痒、头屑和皮脂溢出,而且使用方便无明显不良反应[8]。

2.3. 尿素

尿素具有抗真菌和抗细菌特性, 以及高保湿能力和角质层分离作用。使用角质层分离剂可以防止脂溢性皮炎患者脱屑或结痂, 并可以增加外用药物的渗透性。尿素通过调节角质形成细胞中与其分化和抗菌肽产生相关的基因表达来改善皮肤屏障功能, 包括抗菌防御。它还在调节角质形成细胞增殖中发挥重要作用[9]。Leonardo Celleno 等测试了含有 10%尿素的市售产品对脂溢性皮炎的作用, 结果显示脱屑量和干燥度有显著下降[10]。

2.4. 丙二醇

丙二醇在皮肤科主要作为一种溶剂、角质分离剂和渗透增强剂, 能有效地对抗真菌[11]。丙二醇已被证明可以抑制细菌和/或真菌的生长。丙二醇还被证明对脂溢性皮炎有效[12]。Faergemann 在对比含有 15%丙二醇、50%乙醇和 35%水的溶液及含有 50%乙醇和 50%水的溶液的治疗中, 对其中部分治疗后患者进行了轮状糠秕孢子菌的定量培养。用含丙二醇的溶液处理后, 微生物数量显著减少[13]。

3. 抗真菌药

3.1. 酮康唑

麦角甾醇是真菌细胞膜的重要组成部分。酮康唑通过阻断细胞色素 P450 14- α -脱甲基酶来抑制麦角甾醇的产生, 该酶是从羊毛甾醇产生麦角甾醇所必需的。酮康唑可以改变皮肤脂质分布, 影响马拉色菌脂质代谢并有利于产生生物素的细菌。生物素调节炎症反应和细胞增殖, 有助于症状改善[14]。Draelos 在起始以及第 4、8、16、26、39 和 52 周(或提前终止)时对受试者的不良事件(AE)、严重不良事件(SAE)、目标病变红斑、鳞屑和瘙痒进行评估, 以及研究者的静态整体评估(ISGA)分数, 得出 2%酮康唑泡沫对于脂溢性皮炎患者的长期安全性良好, 且疗效得以维持[15]。Peter 等人验证 2%酮康唑洗发水非常有效, 不仅可以清除头皮脂溢性皮炎和头皮屑, 而且每周预防性使用一次还可以预防疾病复发[16]。

3.2. 二硫化硒

二硫化硒可以减少头皮过度脱屑和瘙痒, 减少角质层中的细胞粘附。作为药物抗有丝分裂机制的一部分, 胸苷掺入表皮细胞 DNA 的速率降低, 从而降低了表皮细胞更新的速率。Gabriela Turcu 等对超过 1281 名有头皮屑或 SD 的受试者进行的观察性现实生活研究的结果证实, 定期使用二硫化硒的洗发水超过 4 周可显著减少该病症的临床体征和症状, 并减少其对头皮的影响[17]。Philippe Massiot 等研究在经过 2 周的皮质类固醇/水杨酸初始治疗后, 每周一次二硫化硒洗发水治疗中重度头皮脂溢性皮炎, 可显著减少中度至重度头皮脂溢性皮炎的复发[18]。

3.3. 吡啶硫酮锌

吡啶硫酮锌(ZnPT)能够增加真菌细胞中铜的含量, 从而降低铁硫蛋白的功能[19] [20]并使膜去极化, 从而阻止营养物质的移动和能量的产生[21] [22]。ZnPT 会导致酵母细胞内锌水平升高[23] [24], 从而导致金属错位和细胞应激[6]。ZnPT 通过诱导膜去极化来抑制酵母生长所需营养物质的膜运输。ZnPT 可以降低对脂质分解至关重要的脂肪酶表达, 并下调克雷布斯循环成分(例如琥珀酸脱氢酶和柠檬酸合酶)和电子传递链(例如, ATP 合酶亚基)[24]。ZnPT 是非处方制剂中最常用的 SD 治疗剂。ZnPT 作为外用制剂的成功部分归因于它在抗真菌效力、经济性和可用性之间取得的平衡[25]。与硫化硒和焦油不同, ZnPT 还具有无色无味的优点, 使 ZnPT 洗发水成为替代普通非药物洗发水的理想选择, 不仅可以治疗而且可以

预防 SD 再次发生[26]。

4. 抗炎药物

4.1. 糖皮质激素

糖皮质激素, 具有抑制皮肤炎症的功效。Hyoseung Shin 进行了比较外用他克莫司与外用糖皮质激素和吡啶硫酮锌洗发水治疗头皮脂溢性皮炎的研究, 倍他米松洗剂在 4 周内迅速减少了包括头皮屑在内的炎症症状。但是长期外用糖皮质激素会导致皮肤萎缩和毛细血管扩张。如果停止使用倍他米松洗剂, 临床症状可能会复发并加重。因此, 认为外用糖皮质激素不适合作为头皮脂溢性皮炎的单一疗法。外用糖皮质激素对于短期治疗头皮脂溢性皮炎非常有用。但由于副作用, 长期坚持使用比较麻烦。此外, 如果停止使用, 大多数患者会复发[27]。Ortonne 等人比较丙酸氯倍他索洗发水联合酮康唑洗发水有效安全治疗中重度头皮脂溢性皮炎, 发现每周两次丙酸氯倍他索洗发水与每周两次酮康唑洗发水交替联合治疗中重度头皮脂溢性皮炎的疗效明显优于单独酮康唑洗发水, 且效果持续[28]。

4.2. 钙调磷酸酶抑制剂

外用钙调神经磷酸酶抑制剂也具有抗炎作用。它们通过抑制钙调神经磷酸酶(一种与 T 细胞激活相关的钙结合蛋白)来抑制 T 细胞激活和炎症细胞因子的产生。Hyoseung Shin 进行了比较外用他克莫司与外用糖皮质激素和吡啶硫酮锌洗发水治疗头皮脂溢性皮炎的研究, 在 4 周的治疗阶段, 外用他克莫司与强效外用糖皮质激素一样有效, 并且比吡啶硫酮锌洗发水更有效。与外用类固醇相比, 外用他克莫司即使长期使用也不会出现皮肤萎缩、毛细血管扩张等不良反应[27]。Rigopoulos 等人进行 1%吡美莫司乳膏与 0.1%倍他米松乳膏治疗脂溢性皮炎的比较, 吡美莫司和倍他米松治疗脂溢性皮炎均疗效显着。倍他米松比吡美莫司更快地减少红斑、鳞屑和瘙痒这三个参数, 但减少的差异没有统计学意义。与吡美莫司相比, 倍他米松的复发更频繁且更严重[29]。

4.3. 甘草次酸及其衍生物

甘草次酸及其衍生物具有广泛的生物和药理活性, 包括通过减少肿瘤坏死因子(TNF)- α 的产生和抑制核因子 κ -轻链(NF- κ B)活化以及磷酸肌醇 3-激酶(PI3K)活性的抗炎和抗过敏作用[30] [31]。Hsiao-Chi Wang 等对 34 名患者入组并接受 6%甘草次酸复合洗发水治疗。由同一位皮肤科医生在用药前, 用药第 2 周和第 5 周根据皮肤科生活质量指数(DLQI)和头皮粘附剥落评分(ASFS)对疗效进行临床评估。研究表明 6%甘草次酸复合洗发水对头皮 SD 有显着的治疗反应[32]。

5. 其他药物

0.3%罗氟司特泡沫: 磷酸二酯酶(PDE)4 抑制剂可能对脂溢性皮炎有效, 因为它能够通过提高环磷酸腺苷水平来抑制脂溢性皮炎病理生理学中涉及的促炎细胞因子[33]。外用罗氟司特正在研究用于长期治疗各种皮肤病, 包括特应性皮炎、头皮银屑病和慢性斑块状银屑病[34]-[37]。Andrew Blauvelt 等人进行的每日一次的罗氟司特泡沫(0.3%)治疗的一次 3 期试验结果表明, 在治疗脂溢性皮炎引起的红斑、鳞屑和瘙痒方面具有良好的疗效、安全性和局部耐受性, 支持进一步研究作为非类固醇局部治疗[38]。

6. 小结

现阶段外用药物治疗头皮脂溢性皮炎仍主要集中在角质溶解剂、抗真菌、钙调神经磷酸酶抑制剂及糖皮质激素, 其余新型药物疗效文献报道较少, 还需要更多的研究。脂溢性皮炎致病机制复杂, 治疗方式多样, 外用药物可以针对头皮脂溢性皮炎的多种致病机制发挥作用, 从而达到治疗效果。并且可以联

合系统治疗和物理治疗, 进一步提升疗效。对于不同患者的皮损情况不同, 需要按照具体情况制定治疗方案, 并及时作出调整。

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