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Updates in therapeutics for folliculitis decalvans: A systematic review with evidencebased analysis.

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Folliculitis decalvans (FD) is the most common neutrophilic scarring alopecia, causing painful, recurrent purulent follicular exudation.¹ Currently, there is a paucity of data regarding the efficacy of FD-specific treatments. This study aimed to provide an evidence-based analysis of current treatment efficacy for FD. Using PRISMA guidelines, PubMed, Medline, SCOPUS and Cochrane library were searched for articles published in English from 1998 to 2018. Data regarding treatment regimen and efficacy was graded according to the American College of Physicians grading system.²

Treatment efficacy of FD was discussed in 20 studies including 282 patients, of which 73.4 % were male. The highest level of evidence was Grade 3, encompassing seven studies with 263 patients. A multicenter retrospective study showed that 15 patients treated with a 10-week course of clindamycin and rifampicin achieved the longest disease remission at an average of 7.2 months. Remission period was shorter among those treated with doxycycline or azithromycin for 3–6 months, who subsequently received adjunct topical antibiotics and intralesional corticosteroids.³ Powell et al., demonstrated that a 10week course of clindamycin and rifampicin achieved remission in 10/18 patients (55.6%) for 2–22 months, and 5 additional patients responded to 2–3 more courses.⁴ Similarly, Miguel Gomez et al. demonstrated a 91% response rate and longer duration of response (5 months) in cases initially refractory to tetracycline treatment.⁵ Conversely, a retrospective study by Tietze et al. showed 8/12 patients treated with a 10-week course of clindamycin and rifampicin relapsed and 2 had no clinical response.⁶

In another retrospective study, 7/10 patients treated with combination tetracycline, clobetasol lotion and intralesional triamcinolone (ILT) for average of 7 months, were in disease

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remission for up to four years. Continued treatment with oral antibiotics, ILT or clobetasol lotion was needed in 11/23 patients to maintain remission.⁷ Tietze et al., demonstrated that isotretinoin (IST) treatment for 5–7 months resulted in disease remission for 4–24 months in 9/10 patients, 3 of whom required low dose maintenance. Of note, treatment of FD with IST was associated with hyperlipidemia (14/39) in another retrospective review.⁸

Newer therapeutic options have been described in case reports and case series in recent years, and accordingly the level of evidence is very low (Grade 4). Red light photodynamic therapy (PDT) resulted in clinical improvement in 9/10 patients, with 6 patients exhibiting disease remission.¹ Additional treatments with lowest evidence were tacrolimus ointment, external beam radiation, isotretinoin, human immunoglobulin, adalimumab, infliximab, long-pulse ND:Yag.

Overall, all studies evaluated had small sample size, lacked control groups, and randomization. Additionally, given the retrospective nature of included studies, blinding was not possible so observer bias may have occurred. Combination of clindamycin and rifampicin was the most commonly used treatment in reviewed studies. However, based on low quality of evidence, we are unable to discern whether it is the most efficacious treatment. The lack of higher grade evidence highlights the need for stronger studies performed to assess the efficacy of various treatments used for folliculitis decalvans, though the rarity of FD makes this challenging.

Supplemental Figure 1. American College of Physicians Treatment Grading Guidelines.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

(FD)	Folliculitis decalvans
(PDT)	Photodynamic therapy
(CS)	Corticosteroids
(IVIG)	Intravenous immunoglobulin
(MAL)	Methyl aminolevulinate
(CsA)	Cyclosporine
(IST)	Isotretinoin

(ILT)	Intralesional triamcinolone
(Nd:YAG)	Neodymium:yttrium aluminum garnet

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Table 1:

Grade 3 Studies with low quality of evidence

Study design	Previous treatment failure	No. of patients	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
1) Retrospective, multicenter review. [Vano-Galvan et al; J Eur Acad Dermatol Venerol. 2015; 29(9): 1750-57]	Not mentioned	<ul style="list-style-type: none"> Total patients: 82 52 were men. Mean age: 35 years. Severe disease 17(21%) pts. 	<ul style="list-style-type: none"> Doxycycline (39 pts) for 3–6 months. Clindamycin and rifampicin (15 pts) for 10 weeks. Azithromycin (6 pts) 3 times weekly for 3 months 	None	<ul style="list-style-type: none"> • Doxycycline: 90% improvement, remission (mean: 4.8 months). • Clindamycin and rifampicin: 100% improvement, remission (mean: 7.2 months). • Azithromycin: 100% improvement, remission (mean: 4.6 months). 	Grade 3
2) Retrospective, single center, observational study. [Tietze et al; J Eur Acad Dermatol Venerol 2015; 29(9):1816-21]	Clindamycin, rifampicin, clarithromycin, dapsone,	<ul style="list-style-type: none"> Total patients: 28 26 were men. Age range: 19–64 years. 	<ul style="list-style-type: none"> • IST (0.2–0.5mg/kg) for 5–7 months. • Dosage tapered after remission achieved to 10mg 2–3 times weekly in 3 patients. • Follow-up period range: 2 months 15 years 	None	<ul style="list-style-type: none"> • Complete remission with IST in 9 (90%) pts for 4 months – 2 years. 3 (30%) patients required maintenance on low dose IST. • Relapse rates with antimicrobials: clindamycin/rifampicin 8 (80%) pts, clarithromycin 6 (67%) pts, ciprofloxacin or doxycycline 7 (78%) pts, dapsone 4 (57%) pts. 	Grade 3
3) Retrospective, single center, observational study. [Bunagan et al; J Cutan Med Surg. 2015; 19(1):45-9]	Not mentioned	<ul style="list-style-type: none"> Total patients: 23 16 were men. Follow-up period ranged between 3 months to 13 years. 	<ul style="list-style-type: none"> • ILT + Clobetasol lotion + (either doxycycline 100mg bid, minocycline 100mg bid or tetracycline 500mg bid) (n=10) • Cephalixin + ILT + clobetasol lotion (n=6) • Clindamycin + rifampicin (n=1) • ILT + clobetasol lotion (n=1) • Multiple combinations (cephalexin, minocycline, tetracycline, rifampicin, clindamycin, ciprofloxacin, IST, dapsone) (n=5) 	None	<ul style="list-style-type: none"> • FD in remission in 7/10 (70%) patients, treatment discontinued. FD inactive in 3 (30%) patients with continued treatment. • FD inactive in 6/6 (100%) patients with continued treatment. • FD in remission in 1/1 (100%) patient, treatment discontinued. • FD in remission in 1/1 (100%) patient, treatment discontinued. FD under control in 2/5 (40%) patients with continued treatment. FD still active in 3/5 (60%) patients despite treatment. 	Grade 3
4) Single center case series, Non-blinded, non-randomized study [Sillani et al; Int J Trichol Jan 2010;2(1):20-3]	Not reported	<ul style="list-style-type: none"> Total patients: 13 11 were male Mean age 30.1 range 15–66 	<ul style="list-style-type: none"> • Mild FD - Minocycline 100 mg po twice daily • Moderate FD - Minocycline 100 mg po twice daily + Rifampicin 150–300 mg twice daily. • Adjuvant drugs used included topical fusidic acid or mupirocin, selenium sulfide shampoo, oral compound glycyrrhizin, and zinc gluconate 	One patient developed nausea and vertigo from rifampicin	<ul style="list-style-type: none"> • Mild FD cases (n=8) - Minocycline 100mg bid, for an average of 5.7 weeks was able to clear inflammatory scalp lesions in 7 out of 8 patients, 1 of whom needed two week Acitretin rescue therapy. 1 of 8 exhibited FD relapse after 8 months. • Moderate FD cases - A combination of Minocycline and Rifampicin for an average of 11.7 weeks was effective in treating three patients. Clarithromycin + Rifampicin for average of 10 weeks was also effective in clearing scalp lesions in 2 patients (1 mild FD, and 1 moderate FD). *9 out of 13 patients were partial hair growth responders (<75%) 	Grade 3
5) Case series study. [Powell et al; Br J Dermatol.1999;140 (2):328-33]	Flucoxacillin, erythromycin, minocycline.	<ul style="list-style-type: none"> Total patients: 18 13 were men. Age range (18–62 years) 	<ul style="list-style-type: none"> • Clindamycin 300mg twice daily and rifampicin 300mg twice daily for 10 weeks. 	One patient developed a rash from clindamycin.	<ul style="list-style-type: none"> • FD in remission for 2–22 months in 10(55.6%) patients after one 10-week course. • FD in remission in 15(83.3%) patients after a further 2–3 10-week course. 	Grade 3
6) Retrospective, multicenter review. [Miguel-Gomez et al; J Am Acad Dermatol. 2018; Epub ahead of print.]	Not reported	<ul style="list-style-type: none"> Total patients: 60 37 were men. Median 40 Age range (23-83 years) 	<ul style="list-style-type: none"> • Topical steroids (n=48) • Topical antibiotics (n=37) • Tetracycline (n=36) • Intralesional steroids (n=25) • Rifampicin and clindamycin (n=21) • Oral isotretinoin (n=15) • Photodynamic therapy (n=8) • Oral steroids (n=5) • Azithromycin and dapsone (n=4) • Topical tacrolimus (n=3) • Hydroxychloroquine and minoxidil (n=2) 	Epigastralgia, diarrhea, and headache were associated with tetracyclines in four patients. Hypercholes terolemia, arthralgias and epistaxis in 3 pts treated with isotretinoin.	<ul style="list-style-type: none"> • Tetracyclines used in moderate and severe FD pts (n=36) had a 91% response rate. • In refractory cases, the combination of rifampicin and clindamycin was the most effective with 90.5% response rate, and had longer duration of response at 5 months. 	Grade 3
7) Retrospective, case series study. [Aksoy et al; Int J Dermatol. 2018; 57(2):250-253]	Not reported	<ul style="list-style-type: none"> Total patients: 39 male Mean age 37.85 Range (16-82) 	<ul style="list-style-type: none"> • Oral isotretinoin 0.1–1.02 mg/kg/d for a median duration of 2.5 months (range: 1–8months) • Patients that responded to treatment (n=36) were subgrouped according to daily dose (<0.4 mg/kg and 0.4 mg/kg) and duration (<3 mo or ≥3mo) 	Hyperlipidemia (35.9%), intractable xerosis (10.3%)	<ul style="list-style-type: none"> • 36 pts had partial and complete response following isotretinoin treatment • 61.5% of pts had response to IST w/1 month. • 66% of pts receiving IST <3 mo relapsed. Pts that received oral IST 0.4 mg/kg/day for ≥ 3 mo had the best response to IST, and 66% did not have disease relapse. 	Grade 3

Table 2:

Grade 4 Studies with very low level of evidence

Study design	Previous treatment failure	No. of patients	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
1) Retrospective, case report. [Collier et al; Clin Exp Dermatol. 2017; doi: 10.1111/ced.13238]	Doxycycline, rifampicin, clindamycin, IST, acitretin, CS, CsA.	• 26-year old man	• Systemic PDT with ultraviolet light (100–140 J/cm ²) with 1mg/kg porfimer sodium.	• None	• FD in remission at 25 months followup.	Grade 4
2) Retrospective, case series. [Burillo-Martinez et al; J Am Acad Dermatol.2016; 74(4):e69–70.]	Oral and intralesional CS, antibiotics	• Total patients: 3 men • Mean age: 30 years	• PDT • Mean: 11 sessions over mean of 9 months. • Concurrent treatment with sulfamethoxazole-trimethoprim.	• Pain and erythema in all patients. Worsening of condition in one patient.	• 2 patients had mild improvement after PDT session but relapsed before next cycles. • 1 patient had worsening of FD during treatment and required oral CS.	Grade 4
3) Retrospective, case report. [Elsayad et al; Strahlenther Onkol. 2015; 191(11):883–8]	Tetracycline, rifampicin, cefaclor, clarithromycin, linezolid, CS, CsA, IST.	• 45-year old man	• First course radiotherapy: 5 Gy in 5 fractions • Second course radiotherapy: 6 Gy in 5 fractions 5 months later.	• Mild pain, erythema and transient increased scalp exudate.	• FD and associated symptoms significantly improved especially pain and pruritus at 12 months follow-up.	Grade 4
4) Prospective, single center, case series. [Miguel-Gomez et al; J Am Acad Dermatol. 2015;72(6): 1085–7]	Doxycycline, IST, rifampicin.	• Total patients: 10 • 5 were men.	• PDT with MAL (Metvix) 160mg/g cream at 4 week interval. • Area treated with a red light at 630nm with a total light dose of 37 J/cm ² . • 2 patients received concurrent doxycycline and intralesional CS.	• 6 (60%) patients experienced local reaction post-PDT and pain.	• FD in remission for 9 (90%) patients. Duration of remission ranged from 2 to 36 months (mean 9.9 months). • No. of pts and (no. sessions): • 1(13), 1(9), 1(6), 1(5), 3(4), 1(3).	Grade 4
5) Retrospective, case report. [Ismail et al; J Dermatolog Treat 2015; 26(5):471–2]	Clindamycin, rifampicin	• 27-year old man	• IVIG 2g/kg first month then reduced to 1g/kg from second to fourth month. • Concurrent flucloxacillin up to 3 infusions.	None	• FD in remission at 6 months followup.	Grade 4
6) Retrospective, singlecenter, case series. [Kreutzer et al; J Dtsch Dermatol Ges 2014;12(1):74–6]	Clindamycin, rifampicin, dapsone, methotrexate, oral CS, IST.	• Total patients: 2 women • Age (58 and 50 years)	• Adalimumab 40mg every 2 weeks.	None	• FD in remission after 2–3 months of treatment. Long term follow-up unavailable.	Grade 4
7) Case report. [Meesters et al; J Dermatolog Treat	Tetracycline, Erythromycin, Doxycycline, Flucloxacillin, IST.	34-year old man	• Long-pulsed Nd:YAG 1064-nm laser. • Started at 30J/cm ² for 50ms. Dose	• Pain and mild crusting but relived with topical lidocaine ointment and oral tramadol 50mg during treatment.	• FD in remission at 1.5 years followup.	Grade 4

Study design	Previous treatment failure	No. of patients	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
2014;25(2): 167–8]			increased to 50J/cm ² with reduced pulse duration to 30ms. • Total of 9 treatments, 8–12 week interval.			
8) Retrospective, case report. [Mihaljevic et al; J Dtsch Dermatol Ges 2012; 10(8): 589–90]	IST, oral CS, oral antibiotics, dapsone and zinc.	45-year old man	• Infliximab 5mg/kg every 46 weeks.	None	• FD in remission after 3 infusions until 12 months follow-up.	Grade 4
9) Retrospective, case report. [Castano-Suarez et al; Photodermatol Photoimmunol Photomed. 2012; 28(2): 102–4]	Topical CS, IST, Dapsone	32-year old woman	• PDT with MAL (Metvix) • 630 nm delivered at 37J/cm ² ; 3 cycles over 8 week period. Each cycle involved 2 treatments with 2 weeks apart.	Mild itching	• FD in remission at 12 months followup after last treatment.	Grade 4
10) Retrospective, case series. [Bastida et al; Int J Dermatol. 2012;51(2): 216–20]	Acitretin, dapsone, oral and topical CS, antibiotics	• Total patients: 4 • 3 were women • Age (23–40 years)	• Tacrolimus (0.1%) ointment twice daily. • One patient had combination treatment with doxycycline 100mg daily.	None	• FD in remission at follow-up (range 2 months - 2.5 years). • Relapse occurred shortly after treatment discontinued.	Grade 4
11) Retrospective, case report. [Parlette et al; Dermatol Surg. 2004;30(8): 1152–4]	Dicloxacillin, tetralsal, doxycycline, minocycline, Levofloxacin, ILT, IST. One course of Radiation.	26-year old man	• Nd:YAG laser at 28 J/cm ² , 3msec pulse duration, a 12mm spot, and dynamic cryogen spray cooling set at a 50-msec spray and a 20-msec delay. • Patient received 8 treatments at 4- to 6-week intervals.	Significant pain during treatment	• FD in remission at 6 months followup.	Grade 4
12) Retrospective, case report. [Gemmeke et al; Acta Dermatovenerol Alp Pannonica Adriat. 2006; 15(4):184–186.]	Prednisolone and ampicillin	27-year old man	• Isotretinoin 30mg daily, Oral clindamycin 300mg/d for 6 weeks, Prednisolone 20mg daily tapered within 3 weeks.	None	• At 3 weeks, marked reduction in inflammation and partial regrowth in non-scarred scalp areas. • At 6-month follow-up, no disease progression was noted.	Grade 4
13) Retrospective, case report. [Kaur et al; J of Dermatol. 2002;29(7): 180–181.]	Multiple short courses of low dose corticosteroids and antibiotics	42-year old male	• Rifampicin 600 mg PO once daily • Topical 2% Mupirocin ointment	None	• At 2 weeks, pain and folliculitis disappeared, and no new pustules formed. • Alopecia did not extend but scarring persisted. • Complete resolution of FD at 6-month follow up.	Grade 4

Study design	Previous treatment failure	No. of patients	Treatment regimen	Treatment adverse effects	Treatment outcome	Outcome from ACP grading
14) Retrospective, case report. [Kunte et al; J Am Acad Dermatol. 1998;39(5 Pt2): 891–3]	Flucloxacillin, IST, topical superpotent CS.	27-year old man	• Dapsone 100mg daily	None	• FD in remission for 18 months.	Grade 4

Abbreviations: FD: Folliculitis decalvans, PDT: Photodynamic therapy, CS: Corticosteroids, IVIG: Intravenous immunoglobulin, MAL: Methyl aminolevulinate, CsA: Cyclosporin, IST: Isotretinoin, ILT: Intralesional triamcinolone, Nd:YAG: neodymium:yttrium aluminum garnet

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