Clinical trial

Treatment of persistent alopecia areata with sulfasalazine

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Abstract

Background Alopecia areata is an autoimmune disease with no definitive treatment, and some cases persist despite standard therapies. Sulfasalazine has been reported to show success in the treatment of persistent cases of alopecia areata.

Objective To assess the efficacy of sulfasalazine in cases of recalcitrant alopecia areata that do not respond to topical and intralesional corticosteroids, 5% minoxidil, or psoralen plus ultraviolet-A (PUVA) therapy.

Methods Thirty-nine patients with persistent alopecia areata received 3 g of oral sulfasalazine for 6 months, and terminal hair regrowth was quantified as no response, moderate response, or good response.

Results A good response occurred in 10 of the 39 patients (25.6%), a moderate response in 12 (30.7%), and a poor or no response in 17 (43.5%).

Conclusion Sulfasalazine can be used as an alternative drug in patients with persistent alopecia areata.

Introduction

Alopecia areata is a common disease that is characterized by the rapid onset of nonscarring hair loss in one or several round or oval patches. Sometimes, alopecia areata occurs with extensive or total loss of scalp or body hair.

Alopecia areata is thought to be a T-cell-mediated autoimmune disease directed against an unknown autoantigen of the hair follicle. There is a genetic predisposition underlying alopecia areata; environmental triggers have not been identified.[1] In some cases, there may be spontaneous hair regrowth in limited patches, but in other cases treatment is required. Treatment may be effective in some cases, but others are recalcitrant to all forms of standard therapy. A variety of therapies have been considered for this disease, including corticosteroids (topical, intralesional, or systemic), 5% minoxidil, anthralin, photochemotherapy, contact immunotherapy, ciclosporin, and other measures, none of which have yielded constant results. Sulfasalazine is an anti-inflammatory agent. It is a pro-drug that is not active in its ingested form. Sulfasalazine is degraded by bacteria in the colon into two products: 5-aminosalicylic acid (5ASA) and sulfapyridine. There is some controversy as to which of these two products is responsible for the activity of sulfasalazine. Sulfasalazine has both an immunosuppressive and an immunomodulatory effect. Amongst its activities, sulfasalazine is a 5-lipoxygenase inhibitor, and inhibits the release of prostaglandin E-2 and interleukin-2. Sulfasalazine also decreases inflammatory cell chemotaxis, cytokine and antibody production, and probably acts on certain lymphocyte subsets.[2]

Sulfasalazine has been used for the treatment of inflammatory bowel disease, rheumatoid arthritis, and other diseases, including pustular psoriasis, arthropathic psoriasis, psoriasis vulgaris, dermatitis herpetiformis, systemic lupus erythematosus, scleroderma, and acne.

Because of the involvement of T lymphocytes in the pathogenesis of alopecia areata, sulfasalazine may have a role in the treatment of this disease.[3,4] Therefore, we administered sulfasalazine to patients with alopecia areata that was refractory to other therapies.

Materials and Methods

Thirty-nine patients were included in this prospective trial. All patients had some degree of alopecia areata and all had received one or more therapies, including topical and intradermal corticosteroids, 5% minoxidil, and psoralen plus ultraviolet-A (PUVA), for at least 12 months without any results (Table 1). Sulfasalazine tablets were started at a dose of 1 g daily, which was increased to 3 g after 3 months of therapy, and continued for 6 months. The patients did not receive any other additional treatment. Regular monitoring was performed monthly. The results were recorded and analyzed. The modified form of the alopecia severity score, the so-called "Severity of Alopecia Tool" or SALT score, was used. The score was obtained by visual determination of the amount of terminal hair regrowth in each of the four views of

Table 1 Duration of disease, duration of previous therapies, and washout period before initiation of sulfasalazine

Patient	Age (years)/sex	Duration of disease (years)	Duration of previous therapies*			Washout period (years)
			Corticosteroids (topical or intradermal)	Minoxidil	Psoralen plus ultraviolet-A	
1	39/female	2	6 months	12 months	6 months	1
2	19/male	3	12 months	12 months	6 months	1
3	17/female	10	2 years†	12 months	–	2
4	40/male	2	1 year	6 months	6 months	1
5	20/female	7	3 years†	6 months	6 months	1
6	28/male	8	4 years†	1 year	–	1
7	16/male	2	1 year	1 year	–	1
8	36/female	2	6 months	6 months	6 months	1
9	19/male	3	1 year	1 year	6 months	1
10	38/male	4	1 year	6 months	6 months	1
11	36/female	2	1 year	6 months	6 months	1
12	15/male	8	4 years†	1 year	–	2
13	28/male	2	1 year	6 months	6 months	1
14	38/male	4	2 years	1 year	6 months	1
15	16/female	8	3 years	1 year	–	2
16	30/male	2	1 year	6 months	6 months	1
17	16/male	5	2 years	1 year	–	1
18	26/male	2	1 year	6 months	6 months	1
19	18/male	3	1 year	6 months	6 months	1
20	28/male	2	1 year	1 year	6 months	1
21	20/female	10	3 years	1 year	6 months	2
22	40/female	3	1 year	6 months	6 months	1
23	18/male	2	1 year	6 months	–	1
24	19/male	3	1 year	1 year	–	1
25	41/male	2	1 year	6 months	6 months	1
26	31/male	2	1 year	6 months	6 months	1
27	20/male	2	1 year	6 months	6 months	1
28	31/female	2	1 year	6 months	–	1
29	16/female	8	2 years	1 year	–	2
30	32/male	2	1 year	6 months	6 months	1
31	21/female	4	2 years	6 months	–	1
32	30/male	2	1 year	6 months	6 months	1
33	35/male	5	2 years	1 year	6 months	1
34	24/male	2	1 year	6 months	6 months	1
35	16/female	2	1 year	6 months	–	1
36	24/male	6	3 years	1 year	6 months	2
37	19/female	3	1 year	6 months	6 months	2
38	18/male	2	1 year	6 months	–	1
39	18/male	10	3 years	6 months	–	2

*Some therapies were prescribed simultaneously.
†Patient received treatment intermittently.

the scalp using the Olsen–Canfield method.[5] Terminal hair regrowth was quantified as 1–29% (no response or a weak response), 30–59% (moderate response), or 60–100% (good to excellent response). Only patients with > 29% terminal hair regrowth were considered to have an objective response (Table 2).

Results

Of the 39 patients, 13 were females and 26 were males. The patients were aged between 15 and 41 years. They were evaluated on a monthly basis and the results were documented. Good results were found in 10 patients (25.6%) and moderate hair regrowth in 12 patients (30.7%). There was no response to sulfasalazine in 17 patients (43.5%). Of the 10 patients with good results, two showed recurrence a few months after hair regrowth, and there were three recurrences in patients with a moderate response. Side-effects occurred during treatment, including dizziness and headache in two patients (5.1%), which resolved on lowering the dose of sulfasalazine, and dyspepsia in eight patients (20.0%), which was treated with antacids.

Table 2 Patterns of alopecia and percentage of hair regrowth

Patient	Pattern of scalp alopecia	Duration of treatment (months)	Hair regrowth (%)
1	Patchy alopecia	6	40
2	Patchy alopecia	6	40
3	Patchy alopecia	6	10
4	Patchy alopecia	6	70
5	Patchy alopecia	6	80
6	Alopecia totalis	6	5
7	Alopecia totalis	6	5
8	Alopecia totalis	6	40
9	Patchy alopecia	6	20
10	Patchy alopecia	6	60
11	Patchy alopecia	6	90
12	Patchy alopecia	6	10
13	Patchy alopecia	6	0
14	Patchy alopecia	6	5
15	Patchy alopecia	6	50
16	Patchy alopecia	6	40
17	Alopecia totalis	6	80
18	Patchy alopecia	6	70
19	Patchy alopecia	6	50
20	Patchy alopecia	6	20
21	Patchy alopecia	6	50
22	Patchy alopecia	6	0
23	Patchy alopecia	6	80
24	Alopecia totalis	6	10
25	Patchy alopecia	6	50
26	Patchy alopecia	6	30
27	Patchy alopecia	6	100
28	Alopecia totalis	6	20
29	Alopecia totalis	6	20
30	Patchy alopecia	6	50
31	Patchy alopecia	6	70
32	Patchy alopecia	6	20
33	Patchy alopecia	6	0
34	Alopecia totalis	6	5
35	Patchy alopecia	6	50
36	Patchy alopecia	6	20
37	Alopecia totalis	6	10
38	Patchy alopecia	6	90
39	Alopecia totalis	6	50

Discussion

Sulfasalazine is thought to exert its effect on alopecia areata through its activity on T lymphocytes. The current study confirms the results of previous studies that have demonstrated the favorable clinical response to sulfasalazine in patients with persistent alopecia areata.[3,4] Approximately one-quarter of patients (25.6%) responded well to sulfasalazine and acceptable results were achieved. Of the 10 patients with alopecia totalis, one patient showed a very good response and two patients showed a partial (moderate) response. The duration of disease in the patients was between 1 and 10 years. Three of the patients with a weak response (15, 16, and 18 years of age) had disease of long duration with onset in childhood. This observation correlates with previous data indicating that extensive or severe alopecia in childhood is relatively persistent.[6] As with other treatments for alopecia areata, recurrence may be seen. In our patients, the recurrence rate was 25% in both the good and moderate response groups at the 6-month follow-up evaluation.

Therefore, sulfasalazine can be considered as a replacement therapy for persistent alopecia areata. It has a very good effect in some, but not all, cases, and recurrence can occur. The side-effects of treatment with sulfasalazine were not severe in our study. In a short comparison of the risks and benefits of the previous therapies and sulfasalazine, the following points should be considered: (i) minoxidil is a safe drug with minimal complications (including headache and mild dermatitis), but with a limited and delayed onset of response; (ii) PUVA produces certain complications, such as dry skin, pruritus, and ophthalmic disorders, requires more time and money, and shows a good response only in some cases; (iii) topical and intradermal corticosteroids are classic therapies for alopecia areata with a good response in many cases, but with complications such as skin atrophy and folliculitis; (iv) recurrence can occur in all of these therapies.

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