these medications has a side effect of eyelash hypertrichosis.[1-3] One report of a patient with eyelash loss because of AA demonstrated eyelash growth after cutaneous eyelid application of latanoprost.[4] To evaluate the efficacy of these agents in promoting eyelash growth in patients with AA, we conducted a 16-week, randomized, investigator masked, controlled study.

Eligible subjects were adults with AA with greater than 50% bilateral eyelash loss for 6 months or longer. At the initial visit, informed consent was obtained. A dermatologist documented the percentage of eyelash loss, iris color, and periocular pigmentation. Subjects were then evaluated by an ophthalmologist, who conducted an exam with a baseline measurement of intraocular pressure.

Subjects were randomized to receive either latanoprost or bimatoprost. The investigators were masked to the type of medication that each patient received. Subjects applied latanoprost or bimatoprost solution using a cotton-wrapped applicator directly to the affected upper and lower eyelid margins of one eye only, once daily. The application method was sufficient to leave a visibly wet trail of solution on the eyelid margin. The untreated contralateral eye served as the control. Subjects were seen by a dermatologist every 4 weeks for a total of four visits. During each visit, the eyelid margins were examined for evidence of eyelash growth and pigment change. Every 8 weeks, an ophthalmologist performed a slit lamp examination, documented the intraocular pressure, measured eyelash growth, and photographed the eyes and eyelid margins. Eyelash length was estimated using Schirmer exam test strips photographed on the eyelid margin.

Eleven patients completed the study. Cutaneous application of both medications was well tolerated. No subjects experienced change in iris color or periorbital discoloration. There were no significant changes in intraocular pressure. During the study period, no appreciable eyelash regrowth was noted on clinical assessment of eyelid margins or on review of digital photographs.

The absence of $PGF_{2\alpha}$ analogue—induced hair growth by cutaneous cotton-tipped application may be caused by a lack of stimulation or blockage of an essential mediator of hair growth. The concentrations used were the same as those used in management of glaucoma. Perhaps ocular instillation as in glaucoma treatment may be more effective in stimulating eyelash growth.

Studies in murine hair follicles confirm the stimulatory effect of cutaneously applied $PGF_{2\alpha}$ analogues. In macroscopic and histologic evaluation, $PGF_{2\alpha}$ analogues increase hair regrowth on the depilated skin of mice.[5] Although these studies show promise in the ability of $PGF_{2\alpha}$ analogues to stimulate hair growth, the underlying mechanism of action and the optimal method of drug delivery have yet to be elucidated.

Ingrid Roseborough, MD,[a] Hester Lee, MD,[b] Jennifer Chwalek, MD,[c] Robert L. Stamper, MD,[d] and Vera H. Price, MD, FRCP(C)[e]

From the Department of Dermatology, University of Iowa, Iowa City, Iowa[a]; Department of Ophthalmology, Kaiser Permanente Medical Group, Richmond, California[b]; Department of Dermatology, University of Maryland, Baltimore, Maryland[c]; and the Departments of Ophthalmology[d] and Dermatology,[e] University of California, San Francisco, San Francisco, California

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Reprint requests: Vera H. Price, MD, FRCP(C), Department of Dermatology, University of California, San Francisco, 1701 Divisadero St, San Francisco, CA 94115.

E-mail: pricev@derm.ucsf.edu

REFERENCES

1. Johnstone MA. Hypertrichosis and increased pigmentation of eyelashes and adjacent hair in the region of the ipsilateral eyelids of patients treated with unilateral topical latanoprost. Am J Ophthalmol 1997;124:544-7.
2. Mansberger SL, Cioffi GA. Eyelash formation secondary to latanoprost treatment in a patient with alopecia. Arch Ophthalmol 2000;118:718-9.
3. Tosti A, Pazzaglia M, Voudouris S, Tosti G. Hypertrichosis of the eyelashes caused by bimatoprost. J Am Acad Dermatol 2004;51(5 Suppl):S149-50.
4. Mehta JS, Raman J, Gupta N, Thoung D. Cutaneous latanoprost in the treatment of alopecia areata. Eye 2003;17:444-6.
5. Sasaki S, Hozumi Y, Kondo S. Influence of prostaglandin F_2alpha and its analogues on hair regrowth and follicular melanogenesis in a murine model. Exp Dermatol 2005;14:323-8.

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Evaluation of oral zinc sulfate effect on recalcitrant multiple viral warts: A randomized placebo-controlled clinical trial

To the Editor: Viral warts are caused by the human papillomavirus (HPV).[1,2] Because HPV infection is nonlytic, antigen presentation occurs very slowly. HPV infection does not induce inflammatory cytokines; therefore, therapeutic options aimed at

Table I. Changes in serum zinc level according to response to treatment after a 2-month course of zinc sulfate therapy

Patient code	Serum zinc level before treatment (μg/100 mL)	Serum zinc level after 1 month's treatment	Difference	Response	Serum zinc level after 2 months' treatment	Difference	Response	Age (y)	Sex	Site	Type of wart
1	47	178	131	+				8	F	Hand	Plane
2	54	168	114	+				15	F	Face	Plantar
3	61	70	9	−	211	150	+	23	M	Foot	Common
4	45	61	16	−	72	27	+	18	M	Foot	Plane
5	53	169	116	+				9	F	Hand	Plantar
6	68	199	131	+				26	F	Hand	Common
7	54	208	154	+				19	M	Hand	Common
8	69	75	6	−	88	19	−	15	M	Foot	Plantar
9	71	193	122	+				25	F	Face	Common
10	74	79	5	−	82	8	−	11	F	Foot	Plantar
11	53	176	123	+				23	M	Hand	Common
12	44	166	122	+				17	F	Foot	Common
13	58	180	122	+				13	F	Foot	Plane
14	54	58	4	−	188	134	+	20	M	Face	Common
15	64	170	106	+				18	M	Foot	Plantar
16	67	203	136	+				10	F	Hand	Common
17	39	174	135	+				13	F	Hand	Common
18	67	75	8	−	220	153	+	21	M	Hand	Plane
19	47	166	119	+				26	M	Hand	Common
20	44	165	112	+				8	F	Hand	Plantar
21	45	57	12	−	180	135	+	16	F	Foot	Common
22	52	70	17	−	221	168	−	24	F	Foot	Common
23	47	131	84	+				12	M	Face	Plane
24	68	74	6	−	74	6	−	22	M	Hand	Common
25	54	162	108	+				19	M	Hand	Plantar
26	58	64	6	−	178	120	−	24	F	Hand	Common
27	41	50	9	−	67	26	−	16	F	Foot	Plantar
28	56	176	120	+				20	F	Face	Common
29	38	69	31	−	72	34	+	23	F	Hand	Plantar
30	67	197	130	+				11	M	Foot	Common
31	49	56	7	−	60	11	−	27	M	Hand	Common
32	54	201	147	+				10	F	Hand	Plane

+, Positive; −, negative.

modulating the immune system and facilitating the production of cytokines have been proposed.[3]

One immunomodulatory approach involves prescribing zinc, a micronutrient that is necessary for the normal functioning of cells. More importantly, this element modulates DNA- and RNA-related enzymes and is also involved in many immunologic processes. Kitamura et al[4] proposed that Toll-like receptor–mediated regulation of zinc homeostasis influences dendritic cell function.[4] We conducted a randomized, placebo controlled, and double-blinded clinical trial to evaluate the effectiveness of zinc sulfate in the treatment of patients with recalcitrant multiple warts.

Patients were randomly divided into case and control groups. At the beginning of the study, a 5-cc sample of venous blood was taken from each subject to be tested for zinc levels using an atomic absorption spectrophotometery assay. Two additional venous blood samples, at 1 and 2 months after treatment, were also taken. Subjects in the case group were treated with oral zinc sulfate (10 mg/kg to a maximum dose of 600 mg/day) for at least 1 month and for a maximum of 2 months. Patients in the control group received a starch capsule as a placebo treatment.

One month after the conclusion of treatment, a dermatologist reevaluated the patients. Response to treatment was defined as disappearance of all warts without residual scarring. All patients were followed for recurrence for 6 months after the completion of the treatment. $P < .05$ was considered statistically significant.

The zinc sulfate treated group included 32 patients, 18 (56.2%) were female and 14 (43.8%) were male. The mean age was 17.6 $\pm$ 5.44 years. The

Table II. Response to treatment in case and control groups

	Case group (treatment) (n = 32)	Control group (n = 23)	χ^2	*P* value
Response after 1 month	19*	1		
Response after 2 months	6	2	2.389	—†
Total	25	3		

$\chi^2_{0.025,\,1} = 5.024$ $\chi^2_{0.05,\,1} = 3.84$ $\alpha = 0.1$ $\chi^2_{0.1,\,1} = 2.7055$.
*Number of patients responding to therapy.
†In the above table, because two values were less than 5, we could not define the *P* value; therefore two critical zones are introduced instead.

duration of disease was 28.4 ± 8.08 months. The mean value of zinc in patients' sera at baseline was 55.09 ± 10.07 μg/100 mL. None of the patients showed signs or symptoms of zinc deficiency.

Nineteen (59.3%) of the patients responded completely after 1 month of treatment. The mean value of zinc in those who responded increased to 177.5 ± 19.1 μg/100 mL. The mean serum zinc level after 1 month of treatment in those who did not respond to treatment was 66 ± 8.97 μg/100 mL. In these remaining 13 patients, treatment with oral zinc was continued. Eventually, 6 patients responded completely, while the remaining 7 patients failed to respond. Thus, after a 2-month course of treatment with zinc sulfate, the response rate increased to 78.1% (25/32 patients). The mean serum zinc level in patients who responded to treatment increased to 199.7 ± 19.9 μg/100 mL, while in the remainder, the mean serum zinc level was 73.5 ± 9.2 μg/100 mL (Table I). After 6 months of follow-up in those who received oral zinc therapy and responded to the treatment, no instance of recurrence was noticed.

In the control group, 23 patients completed the course of treatment and follow up. There was no significant difference regarding sex ($P = .765$; $\chi^2 = 0.09$), age ($P = .86$; t = 0.18), or duration of disease ($P = .066$; t = 0.437) between the case and the control groups. Improvement in warts was seen in 3 patients (13%) (Table II). The mean value of serum zinc in control patients' sera at baseline was 56.63 ± 8.73 μg/100 mL. This value did not differ significantly between the case and the control groups ($P = .738$; t = 0.33), and did not change significantly with placebo treatment.

Our findings suggest that oral zinc supplementation should be considered as a therapeutic option in the treatment of recalcitrant warts.

Reza Yaghoobi, MD,[a] Afshin Sadighha, MD,[b] and Davood Baktash, MD[a]

Departments of Dermatology at Jondi Shapour University of Medical Sciences,[a] Ahwaz; Research Center of Chemical Injuries, Baqiyatallah University of Medical Sciences,[b] Baqiyatallah, Iran

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Correspondence to: Afshin Sadighha, MD, Research Center of Chemical Injuries, Baqiyatallah University of Medical Sciences, Baqiyatallah, Iran.

E-mail: Afshin.Sadighha@gmail.com

REFERENCES

1. Gibbs S, Harvey I, Sterling J, Stark J. Local treatment for cutaneous warts: systemic review. BMJ 2002;325:461.
2. Al-Gurairi FT, Al-Waiz M, Sharquie KE. Oral zinc sulfate in the treatment of recalciterant viral warts: randomized placebo-controlled clinical trial. Br J Dermatol 2002;146:423-31.
3. Parton AM, Sommerville RG. The treatment of plantar verrucae by triggering cell-mediated immunity. Br J Pod Med 1994;131:883-6.
4. Kitamura H, Morikawa H, Kamon H, Iguchi M, Hojyo S, Fukada T, et al. Toll-like receptor-mediated regulation of zinc homeostasis influences dendritic cell function. Nat Immunol 2006;7:971-7.

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Case letters

Toxic epidermal necrolysis secondary to emergency contraceptive pills

To the Editor: A 28-year-old white female presented to our emergency department with a 3-day history of fever, rash, and sore throat. During the preceding day, she had developed dysuria and conjunctivitis. Although she denied regular medications, she had ingested four contraceptive pills as a single dose (0.125 mg of levonorgestrel and 0.03 mg of ethinyl estradiol each) 5 days before her visit.