Effective Treatment of Seborrheic Dermatitis Using a Low Dose, Oral Homeopathic Medication Consisting of Potassium Bromide, Sodium Bromide, Nickel Sulfate, and Sodium Chloride in a Double-Blind, Placebo-Controlled Study

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Abstract

BACKGROUND: Topical over-the-counter remedies exist to aid in the control of seborrheic dermatitis and chronic dandruff on a superficial level. Low-dose systemic oral nickel and bromide therapy has shown promise in providing improvement and eventual clearing of the disease. OBJECTIVE: The purpose of this study was to further evaluate the effect of an orally administered low-dose, homeopathic mineral therapy (Potassium bromide 1X, Sodium bromide 2X, Nickel sulfate 3X, Sodium chloride 6X) on seborrheic dermatitis and chronic dandruff. METHODS: Forty-one patients with seborrheic dermatitis and/or chronic dandruff were assigned to one of two treatment groups: Active (containing the medication) or placebo (vehicle). Study medication was administered in a placebo-controlled, randomly-selected, double-blind study for 10 weeks. At the end of 10 weeks all patients crossed over to the active medication, under a different label for an additional 10 weeks in an open study format. RESULTS: Twenty-nine patients completed the 10-week blinded portion of the study. After 10 weeks of treatment, the disease state of the active patients improved significantly over that of the placebo patients ($p<0.04$). The placebo patients' condition before and after crossover to active treatment was also evaluated, showing significant improvement ($p<0.01$) 10 weeks after crossing over to active medication. CONCLUSION: Oral therapy using a low-dose homeopathic preparation combining Potassium bromide 1X, Sodium bromide 2X, Nickel sulfate 3X, and Sodium chloride 6X, provides significant improvement in seborrheic dermatitis and dandruff after 10 weeks of dosing.

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Background

Seborrheic dermatitis is a common, chronic, superficial inflammatory disease of the skin, characterized by pruritic, oily, red patches of various sizes and shapes covering inflamed areas of the scalp, face, and ears.[1-3] Other areas are less commonly affected, such as the pre-sternal

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chest. Rarely there is widespread involvement with erythroderma (reddening of the skin). In recent years it has been shown that at least 50 percent of HIV-infected patients have seborrheic dermatitis. Dandruff is thought to be closely related to seborrheic dermatitis, but is less severe. Although the etiology of this disease spectrum is unknown, recent studies have attributed seborrheic dermatitis to the presence and perhaps over-abundance of *Pityrosporum ovale*, a naturally-occurring yeast on the surface of the skin.[4-8] Other researchers consider seborrheic dermatitis to be an inherited primary inflammatory process and *P. ovale* to cause only a secondary aggravation of the condition.[9] Certain features are often suggestive of psoriasis, and many experts believe there is a spectrum of disease with overlap (sebopsoriasis or seboriasis). Conventional treatment includes various non-prescription shampoos (containing tar, zinc pyrithione, selenium sulfide, and/or salicylic acid), topical corticosteroids, and, to control the *P. ovale*, ketoconazole shampoo or cream. Alternative treatments include topical zinc and/or lithium, essential fatty acids, and various B-vitamins.

Objective

Inorganic bromide has been shown to be effective in the treatment of chronic skin conditions such as psoriasis.[10-12] Other authors have discussed the possible role of nickel in the pathogenesis of psoriasis.[13-19] Based on published and unpublished research, we hypothesize there is a primary biochemical defect in patients with seborrheic dermatitis and dandruff, similar to psoriasis, but to a lesser degree.[20] This study evaluates the therapeutic potential of a low-dose oral administration of potassium bromide, sodium bromide, nickel sulfate, and sodium chloride in a homeopathic formulation.

Methods

Study Design

The study design was a placebo-controlled, randomly-selected, double-blind parallel track study conducted at the dermatology offices of Steven A. Smith, MD, in Tulsa, Oklahoma. The active and placebo groups were assigned coded names by the study monitor and randomized in blocks of four. The study investigator was given a list of the randomized, coded dose groups. As patients entered into the study, they were assigned, with no regard to individual characteristics, to the next available randomized, coded dose group on the list. For the first 10 weeks the blinded patients took the assigned study medication and were evaluated at 0, 5, and 10 weeks. At the end of 10 weeks all patients crossed over to the active medication under a separate label for an additional 10-week open study. Double blinding of the study was maintained until all patients completed the first 10-week dosing period. The patients were given a complete history and physical at the beginning and end of the study. Numerous clinical and laboratory parameters were measured at each visit.

Patient Selection

Study patients were recruited from the dermatology practice of Steven A. Smith, MD and by local advertisement. Patients with typical seborrheic dermatitis or dandruff with a minimum of 20-percent affected scalp surface area, a minimum of 20-percent affected face surface area, or a minimum of 20-percent combined affected scalp and face surface area were admitted to the study. Each patient and, if applicable, his/her legal guardian had all risks and possible benefits explained to them in depth. All patients enrolling in the study gave written informed consent. Once admitted to the study, patients were required to discontinue all concomitant seborrhea medications for two weeks before beginning the study and throughout the study. Children under 12 years, patients with inadequate renal function, and women who were pregnant or breast-feeding were excluded from the study. Other papulosquamous diseases (psoriasis, tinea, etc.) were ruled out on clinical and/or laboratory evidence.

Study Medication and Dosage Schedule

The liquid active study medication consists of potassium bromide (3.5 mg/mL), sodium bromide (3.0 mg/mL), nickel sulfate (0.6 mg/mL), and sodium chloride (0.06 mg/mL) in a vehicle of

Table 1. *Seborrhea Area and Severity Index*

1. The area or degree of involvement of the face and scalp are independently rated on a scale of 0-6 as follows:

Degree of Involvement	Rating
<1%	0
1-10%	1
11-20%	2
21-35%	3
36- 50%	4
51- 75%	5
76-100%	6

Area of Face involved (AF) _____
Area of Scalp involved (AS) _____

2. The erythema and scaling of the face and scalp are rated independently according to the following scale:

Severity of the condition:	None	Very Mild	Mild	Moderate	Severe
Rating:	0	1	2	3	4

FACE: Erythema (EF) _____ Scaling (SF) _____
SCALP: Erythema (ES) _____ Scaling (SS) _____

3. The area and severity ratings above are combined in accordance with the following formula to obtain the SASI score for the patient:

SASI = 0.5 (AF) (EF+SF) + 0.5 (AS) (ES÷SS)
SASI = _____(maximum score = 48)

purified water and 20-percent ethyl alcohol (commercially available as Loma Lux Psoriasis™). The placebo formula consisted of vehicle only. No other preservatives or flavor agents were added. With the alcohol flavor masking taste, there were no discernible differences between the study medication and placebo. High purity nickel sulfate hexahydrate, sodium bromide, sodium chloride, and potassium bromide suitable for human use was used in the study medication formulated as a homeopathic medication (Potassium bromide 1X, Sodium bromide 2X, Nickel Sulfate 3X, Sodium chloride 6X) in accordance with the Homeopathic Pharmacopoeia of the United States.[21] Daily dosages were within acceptable dietary intake levels set by various government agencies.

The patients self-administered the study drug on an eight-hour fasted stomach at the beginning of the day, before eating or drinking anything other than water. Only water was consumed for at least 30 minutes after taking the medication. The recommended dosing schedule depended on the patient's weight: up to 100 lbs dosed 2 mL/day, 100-200 lbs dosed 4 mL/day, and over 200 lbs dosed 8 mL/day. Patients consuming 4 mL of the active medication ingested 0.91 mg of inorganic nickel and 18.7 mg of inorganic bromide per day. Compliance was measured by comparing volume of solution returned at next visit to the number of doses theoretically taken based on the daily dosage.

Evaluation of Efficacy and Safety

The primary objective efficacy variable was the percent improvement in Seborrhea Area and Severity Index (SASI) (Table 1). Based on the Psoriasis Area and Severity Index (first described by Fredriksson[22]), the SASI rates both the degree of involvement and severity for seborrheic dermatitis and dandruff on the head as a single number on a scale of 1 to 48. The head is divided into the scalp and facial (including anterior neck and ears) areas that are accorded equal weighting for purposes of the rating formula (as described in Table 1). The criteria for safety of all patients included a satisfactory exam at each five-week visit and satisfactory laboratory results (as compared to baseline lab results) at weeks 10 and 20. In

Table 2. *Age and Gender Distribution at Baseline and 10 Weeks after Starting the Study*

Age Distribution

Week	Dose Group	20<age<40	40<age<60	60<age<80	Row Totals	p-value[a]
0	Active	5	8	7	20	0.5362
	Placebo	6	5	10	21	
Total Week 0		11	13	17	41	
10	Active	3	4	9	16	0.0758
	Placebo	4	7	2	13	
Total Week 10		7	11	11	29	

Gender Distribution

Week	Dose Group	Male	Female	Row Totals	p-value
0	Active	12	9	21	0.4369
	Placebo	9	11	20	
Total Week 0		21	20	41	
10	Active	10	6	16	0.3787
	Placebo	6	7	13	
Total Week 10		16	13	29	

[a]From X^2 test of significance.

addition, any adverse events were recorded, evaluated with regard to possible connections with the study medication, and treated if necessary.

Statistical Analysis

The difference between the percentage change in SASI from baseline for the two different treatments at weeks 5 and 10 was statistically evaluated using the independent t-test. Since the patients who started on placebo medication in the blinded portion of the study also undertook the active treatment during the open phase of the study, the paired t-test was used to evaluate their paired responses before (Week 10) and after crossover (Weeks 15 and 20) to the active study medication. For safety purposes, shifts in laboratory values from baseline to Weeks 10 and 20 were analyzed using repeated measures ANOVA. The X^2 test of significance was used to evaluate differences in frequencies.

Results

Demography

Twenty-four males and 21 females ranging in age from 20 to 77 years (mean age: 53 years) entered the study. Twenty-three patients were randomly assigned to the placebo group while 22 were randomly assigned to the active group. Four patients (3 placebo and 1 active) were excluded by the investigator prior to breaking the double-blind code based on subsequent diagnoses of sebo-psoriasis, leaving 41 patients (21 males and 20 females) in the study. The remaining patients were age- and sex-matched both at baseline and at 10 weeks after excluding all dropouts (Table 2). The baseline seborrheic disease state (as measured by the SASI) was consistent between the placebo and active groups (p=0.2686).

Patient Withdrawal

During the 10-week blinded portion of the study, three placebo and three active patients discontinued the study and were lost to follow-up. Also during this 10-week period, three patients discontinued due to conditions unrelated to the study medication: one active patient discontinued due to a broken leg; one active patient discontinued due to a deteriorating disease condition – excessive flaking and scaling – that caused embarrassment on the job; and one placebo patient discontinued after experiencing facial contact dermatitis due to hair chemicals. Three patients discontinued due to potential side effects (placebo: nausea, flu-like symptoms; active: stomach problems).

Figure 1. *Mean Percentage Change in Seborrhea Area and Severity Index Relative to Baseline for Placebo and Active*

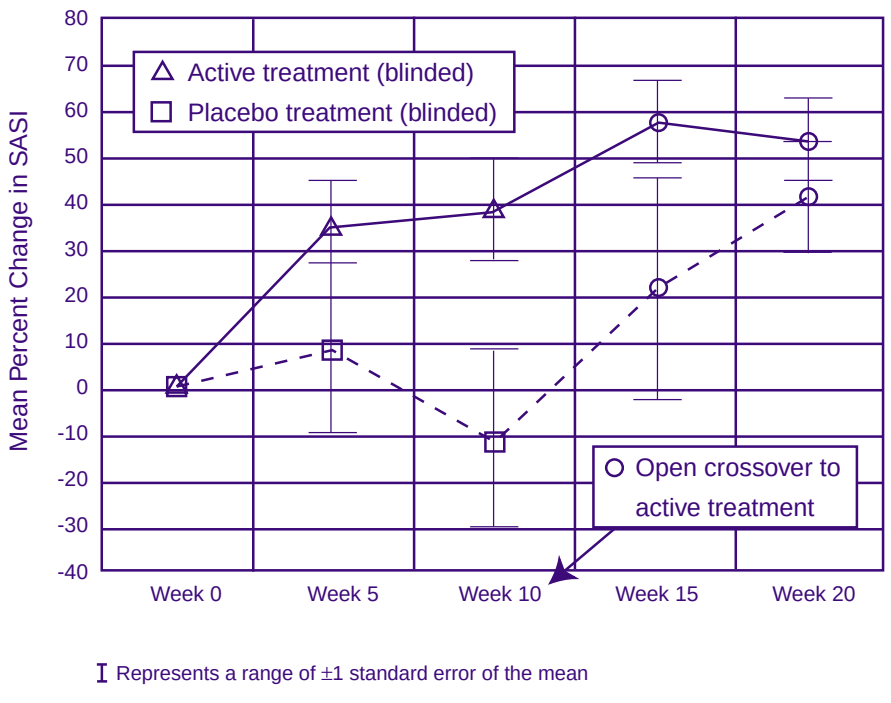


Table 3. *Comparison of Percentage Change in SASI between Placebo and Active Treatment*

Treatment	Placebo	Placebo	Placebo	Active	Active	Active	
Week	Mean	n	Std. Dev.	Mean	n	Std. Dev.	p value
5	8.434	15	68.99467	35.181	17	35.48326	0.1915
10	-10.821	13	66.15631	38.542	16	42.12583	0.0302

Twenty-nine patients (ten active males, six active females, six placebo males, and seven placebo females) completed the 10-week blinded portion of the study. Twenty-one patients (eight active males, three active females, five placebo males, and five placebo females) completed the entire 20-week study.

Efficacy

Overall, the active treatment group responded favorably to therapy throughout the entire 10-week blinded dosing period. See Figure 1 for graphic summary.

A significant difference in percent improvement in SASI between the placebo and active groups was detected at 10 weeks (p=0.0302) (Table 3). At this point, the seborrhea disease state for the active group had improved an average of 38.5 percent while the placebo group's condition worsened (average of -10.82%)

In order to verify the above results, a paired t-test was used to compare the responses of patients in the placebo group before (when on placebo medication) and after crossover to active medication (Table 4).

Table 4. *Comparison of Percentage Change in SASI in Placebo Group before and after Crossover to Active Medication*

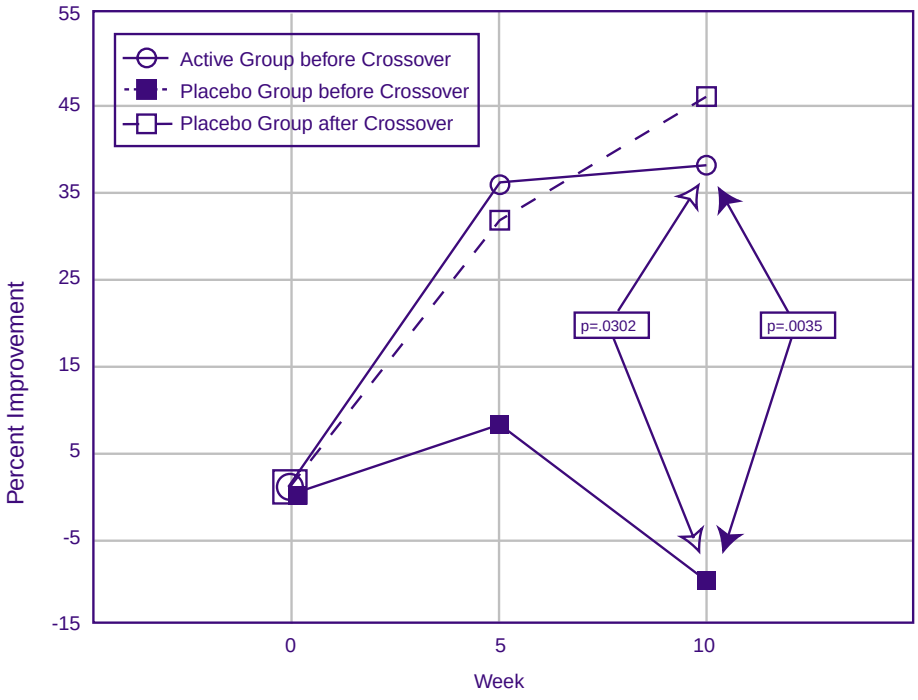
		Placebo		Active		
Week	n	Mean	Std. Dev.	Mean	Std. Dev.	p value
5 vs.15 (1)	11	11.197	60.8351	21.208	79.6993	0.6606
10 vs. 20 (2)	10	-16.400	50.1197	41.643	39.4482	0.0035

(1) 5 vs.15: placebo group 5 weeks after starting placebo treatment vs. placebo group 5 weeks after starting active treatment (Chronologically, week 15 of the study).

(2) 10 vs. 20: placebo group 10 weeks after starting placebo treatment vs. placebo group 10 weeks after starting active treatment (Chronologically, week 20 of the study).

A significant improvement in seborrheic disease state due to the active treatment after crossover did not occur until 10 weeks of active dosing (p=0.0035). These within-group analyses confirm the results from the blinded portion of the study that a significant improvement in seborrheic disease state occurred 10 weeks after starting active treatment. This trend is graphically represented in Figure 2.

Figure 2. *Percentage Change in Seborrhea Area and Severity Index Relative to Baseline for Placebo Group before and after Crossover, and Active Group before Crossover*



For the placebo group after crossover to active treatment (-□-), percent change in SASI was calculated using week 10 SASI scores as baseline (end of placebo treatment). Therefore, actual week 15 translates to 5 weeks on active treatment and actual week 20 translates to 10 weeks on active treatment for purposes of this figure for this group (-□-).

Safety

There was no significant difference (p=0.7999) between the frequency of adverse events for the active group as compared to the placebo group (Table 5). The most frequent adverse events were stomach upset, stomach pain, and nausea, which occurred in 10.4 percent of the active treatment patients compared to 17.7 percent of the placebo patients. These adverse events were mild and infrequent.

Changes in laboratory parameters (standard serum chemistry profile, complete blood count, and urinalysis) over time were evaluated for the active-treatment, placebo-treatment-before-crossover, and placebo-after-crossover-to-active groups. Small but statistically significant (a=0.05) shifts from the baseline occurred for some laboratory parameters in both the active and placebo groups. All significant shifts in mean values remained well within the normal lab reference range and were not considered to be causally related to the study medication. No patient had to be withdrawn or discontinued from the study due to abnormal laboratory tests.

Conclusion

After 10 weeks (blinded), the seborrheic dermatitis condition of the treated patients improved significantly when compared to the condition of patients on the placebo treatment. This improvement in seborrheic disease state was confirmed when the responses of the placebo group patients were compared before and after crossing over to active medication. Here, significant improvement also occurred in a similar pattern 10 weeks after starting the active medication. The timing and degree of the

Table 5. *Most Frequently Reported Adverse Events*

	Active (n=29)[b] Patients		Events	Placebo (n=17) Patients		Events	TOTAL EVENTS
Adverse Event	No.	(%)	No.	No.	(%)	No.	
Stomach upset/ pain/nausea	3	(10.4%)	3	3	(17.7%)	3	6
Hair loss	1	(3.5%)	1	1	(5.9%)	1	2
Brittle/breaking fingernails	1	(3.5%)	1	0	(0%)	0	1
Tender lips	1	(3.5%)	1	0	(0%)	0	1
Kidney infection	1	(3.5%)	1	0	(0%)	0	1
TOTALS	7		7	4		4	11

[a] X^2 test of significance, p=0.7999
[b]Includes patients on active medication before and after crossover to open study.

unblinded patients' improvement on active medication paralleled the blinded active patients, which would tend to rule out bias due to knowledge of treatment medication.

Safety assessments in this study documented only small numbers of relatively mild adverse events in both active and placebo groups that were generally well tolerated. Laboratory evaluations over time also documented an excellent safety profile.

Potassium bromide, sodium bromide, nickel sulfate, and sodium chloride are inorganic soluble mineral salts that disassociate within the gastrointestinal tract and are absorbed in ionic form. Nickel is a group 8-transition mineral, very similar to cobalt and iron. It is absorbed variably and absorption is inhibited by concomitant food and drink.[23,24] Absorbed nickel is primarily excreted in the urine and elimination half-life is about 21 hours.[24,25] Renal clearance is rapid and efficient; nickel is homeostatically regulated and does not accumulate in the body.[26] Ionic bromide, on the other hand, is passively, rapidly, and completely absorbed from the intestine and distributed almost exclusively in the extracellular fluids.[27,28] The kidney eliminates bromide with an elimination half-life of 11-12 days.[28]

The mechanism of action for nickel and bromide therapy is not fully understood. A biochemical theory is proposed whereby a genetic error of nickel-dependent metabolism exists. Of central importance is a nickel-dependent enzyme system that can be therapeutically enhanced in a nickel-rich environment. Various homeopathic materia medicas list bromide as an effective antipruritic agent (Clarke, Boericke, etc.).

This study supports previous findings that oral, low-dose, homeopathic therapy with potassium bromide, sodium bromide, nickel sulfate, and sodium chloride is an effective and essentially side-effect free treatment for seborrheic dermatitis and chronic dandruff. For many suffering with these common maladies an oral medication offers new hope for more effective and convenient therapy.

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