

Pharmacology and Therapeutics

TREATMENT OF HYPERHIDROSIS WITH TOPICAL METHENAMINE

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ABSTRACT: Idiopathic palmar and plantar hyperhidrosis is a relatively common disorder of eccrine sweat gland function. Treatment with glutaraldehyde or formaldehyde, although successful, may cause undesirable side effects. Methenamine is a polycyclic organic compound which releases ammonia and formaldehyde at acid pH. Five per cent methenamine in a firm stick gel, applied daily to one palmar or plantar surface of 109 patients with hyperhidrosis, resulted in significantly less sweating after one month. No patients were sensitized to formaldehyde.

For humans, eccrine sweating is the most important mechanism of heat loss in thermoregulation.¹ This is particularly true in tropical environments where convection and radiation may deliver heat to the body rather than from it.² Disorders of sweat gland function have highlighted their importance. Many in-

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vestigators have studied problems of decreased function.³⁻⁵ In contrast, problems of excessive secretion also exist, the most frequent of which is idiopathic palmoplantar hyperhidrosis.^{6,7} This disabling and socially embarrassing problem is associated with an increased frequency of other important dermatologic conditions, including dermatophytosis,⁷ allergic contact dermatitis⁸ and viral warts.⁹

Previous treatment methods for hyperhidrosis have been partially effective. They have included systemic anticholinergic drugs, iontophoresis, sympathectomy, topical aluminum salts, and topical aldehydes such as formaldehyde and glutaraldehyde.¹⁰⁻¹³ Each treatment has been associated with incomplete success or important side effects and complications.^{7,14}

Methenamine is a 6-carbon, 4-nitrogen compound used for many years to treat bacterial infections of the urinary bladder¹⁵ (Fig. 1). After oral ingestion and renal excretion, the organic chemical is hydrolysed at acid pH in the bladder to ammonia and formaldehyde. Released formaldehyde is toxic to many bacteria, which is the mechanism for urinary tract antiseptis.¹⁵

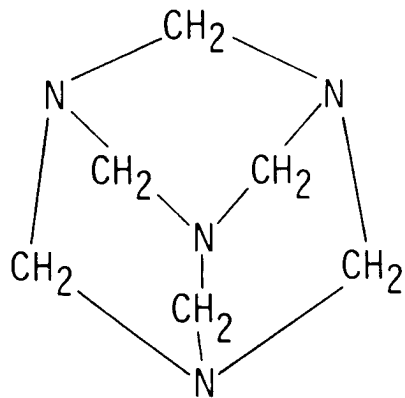
Formaldehyde itself has been used successfully in treating idiopathic palmoplantar hyperhidrosis.¹⁰ Its major disad-

Fig. 1—Acid hydrolysis of methenamine to ammonia and formaldehyde.

vantages have been the use of aqueous solutions, irritant contact dermatitis, and hyperpigmentation or discoloration of the skin.¹¹ The use of topical methenamine in various bases has appeared in the literature.¹⁶ An over-the-counter preparation of 13% methenamine in a gel base is available in Europe. A 5% methenamine in an alcohol gel base preparation has been used. This paper reports its use in 109 subjects with palmar and plantar hyperhidrosis.

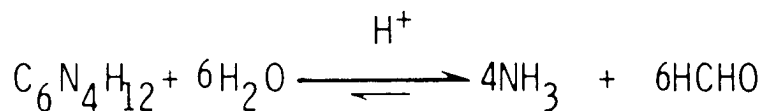
Materials and Methods

Solid sticks containing 5% methenamine were prepared commencing with a 5% methenamine in 5% alcohol gel base composed of glycerine, sodium stearate, and perfume. Identical placebo sticks containing 5% methenamine were likewise prepared. Volunteer patients were selected with moderate to severe hyperhidrosis of the hands or feet. Concomitant topical treatment for hyperhidrosis was not permitted. In a double-



METHENAMINE

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vantages have been the inconvenience of aqueous solutions, irritant and allergic contact dermatitis, and hardening with discoloration of the skin.¹³ Reports on the use of topical methenamine in various bases have appeared in the literature.¹⁶ An over-the-counter preparation of 13% methenamine in an ointment base is available in Europe. A new solid alcohol gel base preparation containing 5% methenamine has been developed. This paper reports its use in treating subjects with palmar and plantar hyperhidrosis.

Materials and Methods

Solid sticks containing 5% methenamine were prepared commercially. They contained methenamine 5%, in a solid alcohol gel base composed of ethanol, glycerine, sodium stearate, dye and perfume. Identical placebo sticks without methenamine were likewise prepared. Volunteer patients were selected with moderate to severe hyperhidrosis of the hands or feet. Concomitant systemic or topical treatment for hyperhidrosis was not permitted. In a double-blind, ran-

dom fashion patients were given one placebo and one methenamine-containing stick. They were instructed to apply one assigned stick to each hand or foot twice daily. Treatment continued for 28 days.

With patients at rest, the amount of accumulated sweat on respective palms or soles was graded clinically on a scale of 0 to 4, with 0 representing a dry extremity and 4 representing excessive amounts of sweat. Observations were made upon entrance into the study and after 28 days of treatment. In addition, decreases in the amount of accumulated sweat on each extremity was assessed on a clinical scale as judged by the investigator after 28 days: excellent improvement, good improvement, partial improvement, no improvement, and worse. A total of 109 patients were evaluated at 7 different dermatology centers. Twenty-five patients have been reported previously.¹⁷

Results

The mean scores for accumulated hand and foot sweat was 3.17 and 3.19 for

studies problems of definition.³⁻⁵ In contrast, probative secretion also exist, the extent of which is idiopathic hyperhidrosis.^{6,7} This disocially embarrassing probated with an increased frequency important dermatologic including dermatophytosis,⁷ contact dermatitis⁸ and viral

treatment methods for hyperhidrosis have been partially effective. Included systemic anticholinergics, iontophoresis, sympathetic ganglionectomy, aluminum salts, and topical agents such as formaldehyde and tannic acid.¹⁰⁻¹³ Each treatment has been associated with incomplete success and side effects and compli-

methenamine is a 6-carbon, 4-nitrogen heterocyclic compound used for many years to treat urinary tract infections of the urinary tract (Fig. 1). After oral ingestion and excretion, the organic chemical is hydrolyzed at acid pH in the bladder to ammonia and formaldehyde. Formaldehyde is toxic to many organisms, which is the mechanism for its use as an antiseptic.¹⁵

Formaldehyde itself has been used successfully in treating idiopathic palmar and plantar hyperhidrosis.¹⁰ Its major disad-

Table 1. Means and Standard Errors of Accumulated Plantar or Palmar Sweat in 109 Patients with Hyperhidrosis*

	Methenamine	Placebo	Difference
Before	3.17 ± 0.069	3.19 ± 0.067	0.02 Not significant
After	1.39 ± 0.110	2.52 ± 0.099	1.13 P < 0.001

* Patients were evaluated before and after treatment with topical 5% methenamine.

methenamine and placebo-treated extremities before treatment (Table 1). After 28 days of treatment, these values had decreased to 1.39 for sides receiving methenamine and 2.52 for sides receiving the placebo. The difference of 1.13 units was significant by a *t*-test of the means and by a *t*-test of the matched pairs data. From this it was apparent that methenamine-treated extremities had significantly less accumulated sweat at rest. This is interpreted as significant improvement in the patients' hyperhidrosis.

A clinical assessment was made of the improvement after 28 days of treatment for each extremity. Table 2 illustrates

Table 2. Clinical Responses of 109 Patients with Hyperhidrosis*

	Methenamine side	Placebo side
Excellent	26	6
Good	45	13
Partial improvement	19	27
No improvement	18	63
Worse	1	0
Total	109	109

* One extremity was treated with topical 5% methenamine, the opposite with a placebo.

the distribution among 5 categorical responses. Seventy-one (65%) methenamine treated extremities were judged as showing good-to-excellent improvement. Ninety (80%) placebo treated extremities were judged as showing no improvement or partial improvement. These differences are significant by the chi-square statistic (chi-square = 27.6; P < .001).

No patient developed allergic contact sensitization to the methenamine or to components of the stick. There were no adverse reactions to the test products and in no instance was it necessary to discontinue treatment prematurely.

Discussion

The mechanism for aldehyde-induced anhidrosis has not been elucidated, but skin stripping experiments imply that it results from eccrine duct blockage in the stratum corneum.¹⁰⁻¹³ Methenamine is stable at physiologic pH, but in fluids which approach pH 5.0, acid hydrolysis of methenamine into ammonia and formaldehyde liberates free formaldehyde. This pH is reached in the stomach,¹⁵ urine¹⁵ and in sweat.¹⁸

Methenamine which is released from the eccrine gland or which is available at the eccrine duct orifice encounters sweat of low pH. Formaldehyde released in relatively high concentration in these locations could explain methenamine's beneficial effect.

No allergic contact sensitization to formaldehyde was observed in any of the patients. This is unusual since topical formalin has been abandoned by some investigators because of the high frequency of sensitization,¹³ and since patients sensitized to formaldehyde may exhibit an eczematous dermatitis on ingestion of methenamine.¹⁹

Methenamine appears to be a safe and effective topical drug in the treatment of palmoplantar hyperhidrosis.

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The subjects developed allergic contact
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and sweat
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Methenamine appears to be a safe and
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Medical Communications

Before you begin to write, ask yourself four questions:

What do I have to say?

Who is likely to pay attention to it?

Where might I get it published for that audience?

Or, in other words, what journal might take it?

How should I say it—write it—for that journal?

And, as a corollary question but an important one, what can I leave out of the paper?—Huth, E. J.: *The Author as Self-Critic, Med. Communications* IV (1):23, 1975.