

# Effectiveness of Ammonium Solution in Relieving Type I Mosquito Bite Symptoms: A Double-blind, Placebo-controlled Study

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**A randomized, double-blind, placebo-controlled study was conducted to compare the efficacy of ammonium solution with placebo in relieving type I symptoms caused by *Aedes aegypti* mosquitoes on 25 healthy subjects. Each subject was bitten once under laboratory conditions by *Aedes aegypti* mosquitoes on the volar aspect of each forearm, and then received the treatment with ammonium solution and placebo, respectively. Compared with placebo, the ammonium solution significantly ( $p < 0.0001$ ) decreased itching/burning/pain immediate type symptoms from 5 to 90 min. Complete and partial relief of the symptoms was noted in 64% in the ammonium solution group compared to none in the placebo group. Key words: *Aedes aegypti*; mosquito allergy; topical treatment.**

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The typical skin response to a mosquito bite in man is seen as an immediate wheal and flare reaction (type I hypersensitivity) followed within 24 h by a delayed papular reaction (type IV) often accompanied by intense pruritis (1). Reaction to mosquito bites is due to an allergic response to the salivary fluids injected by the mosquito (2, 3). An individual can have an immediate response (type I), a delayed response (type IV), a combination of an immediate and a delayed response, or no response at all. The immediate type itching and/or pain and/or burning are common and usually disappear within a few hours (2).

Topical treatment with over-the-counter (non-prescription) agents containing antihistamines, hydrocortisone or other antipruritic agents have been used, but few were controlled studies (4–6).

A dilute form of ammonium solution (3.6%) to relieve the symptoms of itching and pain/burning associated with the bite or sting of insects has been marketed since 1975. The study presented here defines its subjective efficacy.

## SUBJECTS AND METHODS

### *Subjects selection*

The test panel consisted of 25 healthy adult male and female volunteers, aged 18–55 years. The subjects confirmed verbally that they have an immediate response itching and/or burning associated with mosquito bites. Subjects with a history of extracutaneous hypersensitivity to stings by mosquitoes, bees, or wasps, etc., were excluded, as were those taking systemic antihistamines, corticosteroids, or non-steroidal anti-inflammatory drugs (NSAIDs) up to 2 weeks before the experiment. Some subjects experienced bites without any sensation of itching or burning; these subjects were not included. Subjects provided

informed consent, and the study was approved by the Institutional Review Board.

### *Mosquitoes*

Laboratory-reared 7 to 10-day-old *Aedes aegypti* mosquitoes had never been blood-fed and thus were unable to transmit any diseases. They were reared according to standard methods (4).

### *Medication*

Dilute form of ammonium solution (Tender Corporation, Littleton, NH) contained 3.6% ammonium solution and 2% mink oil, and the control contained water (H<sub>2</sub>O) and 2% mink oil.

### *Procedures*

Each subject was exposed to the *Aedes aegypti* mosquito for 10 min. The biting insect was allowed, in 2" × 3" × 1" biting cages, to bite the forearm at one site on the volar aspect of each arm. The actual bite was confirmed visually. Treatment was randomized as to right and left arms; each subject received both samples. The test material was applied from the applicator 5 min after the mosquito bite was confirmed by the subject as itching and/or pain/burning. Subjects signaled any alteration of itching and/or pain/burning, and the time noted; when no relief was reported after 5 min, or if itching/burning/pain returned within 15 min, a second treatment was applied. Degree of relief was scored as: Complete = total relief; Partial = intermediate relief; or None = no relief.

The investigators noted the intensity of the reaction (none, mild, moderate, severe) and the onset of relief, as well as the duration and/or eventual cessation of symptoms. The experimental observation was for 90 min.

The laboratory room was impregnated with the scent of ammonia and the test subjects, as well as the investigators, wore nose clamps to mask the smell of ammonia. Side effects of subjective symptomatology volunteered by a subject were noted and recorded for 24 h, as to the type of severity.

The study was double-blind, randomized, and placebo-controlled. Statistical analysis was performed using the  $\chi^2$  test.

## RESULTS

Of the 25 subjects, 64% experienced complete relief without the return of symptoms, while 36% experienced partial relief in which symptoms did not return for 15 to 90 min after a single application. In contrast, no subjects treated with placebo reported complete relief, while 48% reported partial relief, in which symptoms returned after 15 to 30 min after a single treatment and 60% required two treatments for partial relief. A total of 52% reported no relief from symptoms even after two treatments with placebo. Analysis on relief from symptoms in the pooled data set showed that the efficacy of the ammonium solution was significantly ( $p < 0.0001$ ) superior to placebo treatment. The intensity of reaction was not affected (data not presented). There was no irritation observed as a result of either treatment.

## DISCUSSION

We chose the *Aedes aegypti* mosquitoes because this species is widely distributed (4). The immediate mosquito-bite symptoms (type I) are generally considered to be IgE-mediated and histamine-mediated (5, 6). Oral antihistamines, cetirizine and ebastine significantly reduced immediate pruritus and whealing (5, 6). Ammonium solution has been categorized as category I (safe and effective). The mechanisms of action are unknown.

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