

Ice Cube Test in Children with Cold Urticaria

Nualanong Visitsuntorn, Montri Tuchinda, Napa Arunyanark and Sirikul Kerdsomnuk

Cold urticaria is the common physical urticaria and can be harmful. The occurrence in children is relatively common. A previous study in Thai children with urticaria showed that 1.4% of cases developed symptoms when exposed to the cold.¹ The diagnosis of cold urticaria is mostly based on the history of symptoms after cold exposure. Cold stimulation by ice cube is a simple and popular test to confirm the diagnosis of cold urticaria.² When skin of patients with cold urticaria comes into contact with cold stimuli, mast cells in the dermis are stimulated and release mediators, especially histamine.^{3,4} The wheal and flare usually happen after the skin exposed to the cold becomes warmer.^{2,5} The exact time for the ice cube test is still nonstandardized, varying between 2 and 20 minutes.^{1,2,6,7} The aims of this study were to evaluate in children : (1) the appropriate time for the ice cube test, (2) the sensitivity and specificity of the ice cube test and (3) the effect of cyproheptadine therapy on cold urticaria.

MATERIALS AND METHODS

The study was divided into 2 parts :

SUMMARY The ice cube test performed in 24 children (6 cold urticaria, 6 healthy, 6 allergic and 6 chronic urticaria) showed that a 3 and 5-minute ice cube test was the appropriate time for the diagnosis of cold urticaria without false positive results. If the test was prolonged to 10 and 20 minutes, 17% and 33% respectively showed false positive results in chronic urticaria other than cold urticaria patients. After four weeks of cyproheptadine therapy, the ice cube test showed only 17% positive at 3 minutes and 33% at 5 minutes. When the ice cube test was performed for 10 and 20 minutes, 67% showed positive results. In conclusion, the ice cube test should be performed for 3 to 5 minutes to diagnose cold urticaria in children. The time should be increased to 10 or 20 minutes if the test shows negative results at 3 to 5 minutes after antihistamine therapy.

Part 1. The ice cube test was performed for 3, 5, 10 and 20 minutes on 4 groups of subjects :

group 1 : 6 normal Thai children.

group 2 : 6 allergic patients without episodes of urticaria.

group 3 : 6 patients with cold urticaria, as diagnosed by definite history of repeated urticaria and/or angioedema after exposure to the cold.

group 4 : 6 patients with chronic urticaria whose symptoms were not related to cold exposure.

Each subject had not received any antihistamine for at least 5 days prior to test performing. No subjects had symptoms of urticaria, angioedema, wheezing or rhinorrhea at

the time that the ice cube test was performed.

Part 2. The ice cube test was performed 3, 5, 10, 20 minutes on 6 cold urticaria patients after receiving cyproheptadine 0.25 mg/kg/day (divided into twice daily doses) for 4 weeks.

Ice cube test method

The ice cube test was performed on the ventral surfaces of both forearms as shown in Fig. 1. Four one-

From the Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Correspondence : Nualanong Visitsuntorn

cubic-inch ice cubes were gently placed without pressure on the forearms for 3, 5, 10 and 20 minutes, adding one cube at each of 0, 10, 15 and 17 minutes and removing all at 20 minutes.

The result of the ice cube test was checked at 2 and 10 minutes after the ice was removed and the scores recorded (Table 1) by the same investigator throughout the study. A positive ice cube test is shown in Fig. 2.

Statistical analysis

The results were analyzed by Chi square and student's *t*-tests. A *p* value < 0.05 was considered statistically significant.

RESULTS

Part 1.

Characteristics of the four groups of subjects are shown in Table 2. The ages of the four groups were comparable. The ice cube test results in the four groups of subjects are shown in Fig. 3. The results in normal children (group 1) and atopic children (group 2) were all negative for every period of the time used for performing the test. In cold urticaria subjects (group 3) the positive wheal and flare were found in all of the cases at 3, 5, 10 and 20 minutes. In chronic urticaria subjects (group 4), the ice cube test results at 3 and 5 minutes were all negative but one subject showed a positive result at 10 minutes and two subjects showed positive results at 20 minutes. The wheal and flare score in both subjects was only 1. Wheal and flare scores of ice cube tests in cold urticaria patients are shown in Table 3. In patients 1 and 6, the wheal and flare score obtained after 5 minute ice cube test was 4. When the test was extended to 20 minutes, edema of the forearm from wrist to elbow occurred. The results of the test in two groups of patients with urticaria were compared. The

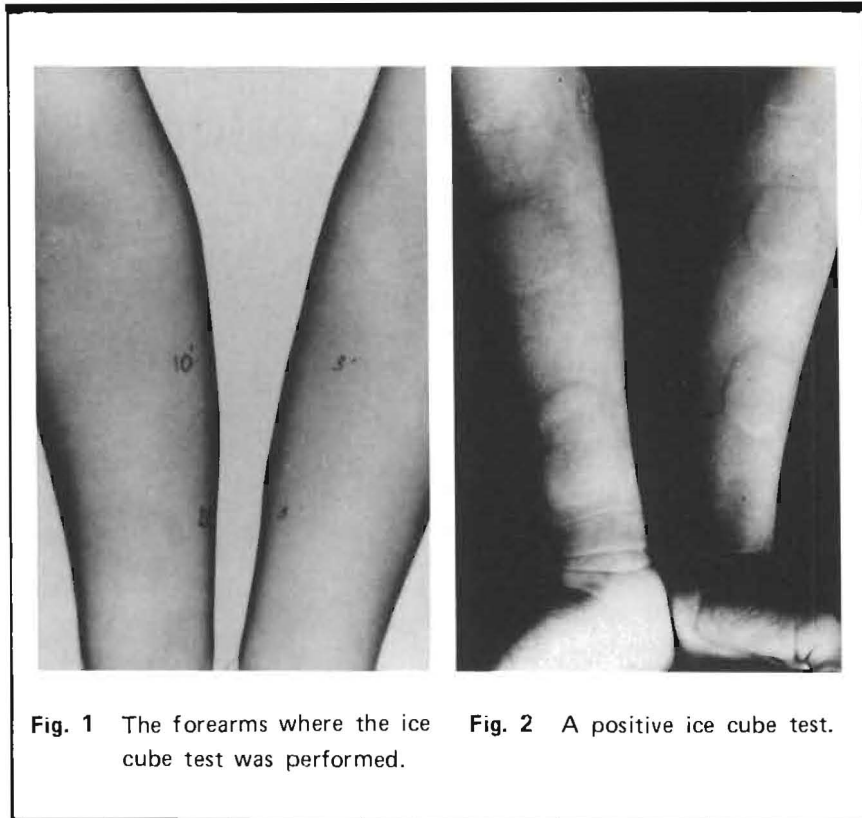


Fig. 1 The forearms where the ice cube test was performed.

Fig. 2 A positive ice cube test.

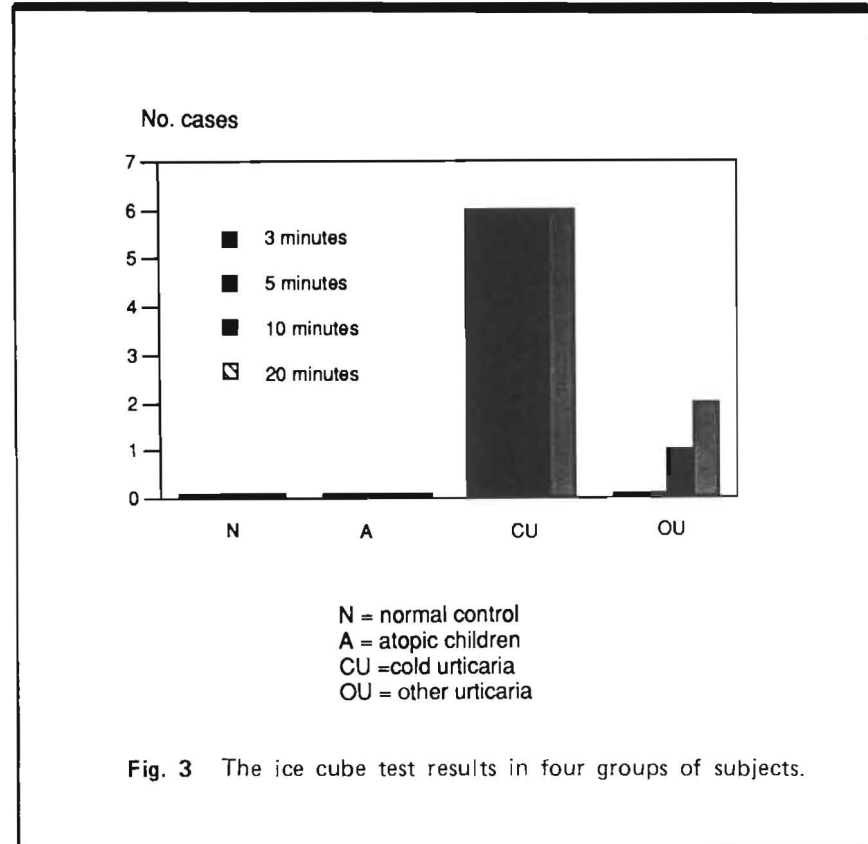


Fig. 3 The ice cube test results in four groups of subjects.

Table 1. Determination of ice cube test

2 min. Pruritus score	
Score	Pruritus symptoms
0	none
1	mild
2	moderate
3	severe

10 min. Wheal and flare score	
Score	Wheal and flare
0	none
1	red, very little edema
2	some wheal, slight raise
3	definite wheal
4	large wheal, 1/8 inch height

Table 2. Characteristics of four groups of subjects.

	Group 1	Group 2	Group 3	Group 4
Number	6	6	6	6
Age (years)	4-8	3-10	4-9	3-10
mean age	6.5	6	7.25	7
Sex				
male	3	4	4	3
female	3	2	2	3
Diagnosis	Normal child	Atopic* disease	Cold urticaria	Chronic** urticaria

* Asthma or allergic rhinitis without episodes of urticaria.

** Patients suffered from urticaria which was not cold urticaria for more than six weeks.

sensitivity and specificity of the ice cube test were calculated by using the previous history of the patients as the gold standard and the results are shown in Table 4. The sensitivity of the test was 100% for every period of the time used for the test. The specificity of the test at 3 and 5 minutes was 100% but it was 83.3% and 66.7% at 10 and 20 minutes respectively.

Pruritus at 2 minutes after the test finished was found only when wheal and flare scores were 2 or more.

Part 2.

After four weeks of cyproheptadine therapy (0.25 mg/kg/day orally), the wheal and flare score was significantly reduced ($p < 0.001$). The wheal and flare scores of the ice cube test after cyproheptadine therapy

are shown in Table 5. The maximal score of the test after therapy was only 1. Positive wheal and flare reactions were found in 1 subject (16.7%) at 3 minutes, 2 subjects (33.5%) at 5 minutes and 4 subjects (66.7%) at 10 and 20 minutes.

DISCUSSION

Cold urticaria is the most common type of physical urticaria. A British study showed that the incidence of cold urticaria was 2.53% of 554 urticaria patients at all age groups and 74% of physical urticaria.⁸ The incidence in Thai children was 1.4%¹ which was lower than the British figure because of the difference in age groups. Cold urticaria is most common in young adults.⁶ Eleven percent of cold urticaria was found before age of ten while 74 percent was found during 10-39 years of age.

The ice cube test is the simplest and easiest investigation to confirm the diagnosis of cold urticaria. The result of the ice cube test is recorded after the skin is warmer. Pruritus is observed at 2 minutes and wheal and flare are observed at 10 minutes after the test. Pruritus is subjective and cannot be statistically evaluated. The wheal and flare score is useful for showing the severity of the result and can be evaluated statistically. In this study, pruritus was observed only when the wheal and flare score was 2 or more. The ice cube test is not always positive in cold urticaria patients.⁹ Ninety percent of cold urticaria patients in any age groups showed positive ice cube tests.⁶ The ice cube test result could be negative when the time is too short or the symptoms are less or have disappeared. If the test is negative but the history is very suggestive, a longer time of exposure to the ice cube, cold water immersion or a cold room may be helpful. If the cold exposure time is too long, systemic reactions may occur in very sensitive cases.¹⁰ The severity of cold sensitivity can be shown with different

Table 3. Wheal and flare score of ice cube test in six cold urticaria patients at 3, 5, 10 and 20 minutes.

Patient No.	Wheal and flare score			
	3 min	5 min	10 min	20 min
1	3	4	4	4*
2	2	2	2	2
3	3	3	3	3
4	2	2	2	2
5	3	3	4	4
6	4	4	4*	4*

* Edema of forearm from wrist to elbow.

Table 4. The sensitivity and specificity of ice cube test for the diagnosis cold urticaria.

Time of ice cube test	Sensitivity*	Specificity*
3 minutes	100	100
5 minutes	100	100
10 minutes	100	83.3
20 minutes	100	66.7

* Sensitivity and specificity was calculated to compare the result in cold urticaria (group 3) and chronic urticaria group (group 4).

Table 5. Wheal and flare score of ice cube test in six cold urticaria patients after four weeks of cyproheptadine therapy.

Patient No.	Wheal and flare score			
	3 min	5 min	10 min	20 min
1	0	1	1	1
2	0	0	0	0
3	0	0	1	1
4	0	0	0	0
5	0	0	1	1
6	1	1	1	1

time duration of the ice cube test.¹¹ The appropriate time for the ice cube test should be long enough to detect cold urticaria but not too long in order to avoid cold induced systemic reactions.

In our study, the sensitivity of the 3, 5, 10 and 20 minute ice cube test for cold urticaria was 100 percent and the specificity was also 100 percent when the ice cube test was done for 3 and 5 minutes. False positive results occurred only in chronic urticaria cases when the ice cube test was done for 10 and 20 minutes and the wheal and flare score was only 1. In two cases of cold urticaria, when the ice cube test time increased to 20 minutes, large local reactions occurred (edema of forearm from wrist to elbow).

There were no false negative ice cube test results in our study compared to 10% in a previous one.⁶ The reason for this difference might be the difference in age, diagnosis and antihistamine therapy. In our study, the patients were all children and the diagnosis was idiopathic cold urticaria without antihistamine therapy. In the previous one, the study was performed on all age groups of any kinds of cold urticaria and the information about antihistamine therapy was not given.

Cyproheptadine is one of the H1 antagonists which is effective in the treatment of cold urticaria^{7,12,13} and showed depression of the ice cube challenge test.¹⁴ In our study, the ice cube test wheal and flare score decreased or was negative in all cold urticaria children after four weeks of cyproheptadine therapy. When the ice cube test time increased to 10 and 20 minutes, there were two more cases that had positive results but the score was only 1.

Most of the patients with urticaria receive antihistamine at the time that the ice cube test is done. To diagnose cold urticaria, antihistamine should be stopped a few days

prior to the ice cube test. If the patient receives antihistamine at the test time and ice cube test is negative at 3 to 5 minutes, the test time should be increased to 10 or 20 minutes to rule out false negative from antihistamine effect.

In conclusion, the ice cube test should be performed for 3 to 5 minutes to diagnose cold urticaria in children but the time may be increased to 10 or 20 minutes if the patients receive antihistamine therapy.

REFERENCES

1. Tuchinda M, Srimaruta N, Habanananda S, *et al.* Urticaria in Thai children. *Asian Pac J Allergy Immunol* 1986; 4 : 41-5.
2. Kaplan AP. Urticaria and angioedema. In Middleton E, Jr., Reed CE, Ellis EF, Adkinson NF, Yunginger JW (eds). *Allergy : Principles and Practice* (3rd ed.) St. Louis, C.V. Mosby Co., 1988, p 1377-401.
3. Soter NA, Wasserman SI, Austen KF. Cold urticaria : reoese into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl. J Med* 1976; 294 : 687-90.
4. Kaplan AP, Gray L, Shaff RE, *et al.* *In vivo* studies of mediators release in cold urticaria and cholinergic urticaria. *J Allergy Clin Immunol* 1975; 55 : 394-402.
5. Fineman SM. Urticaria and angioedema. In Lowlor GJ Jr, Fischer TJ. *Manual of Allergy and Immunology : Diagnosis and therapy* (2nd ed). Boston, Little, Brown and Co., 1988, p 214-24.
6. Neittaanmaki H. Cold urticaria : clinical findings in 220 patients. *J Am Acad Dermatol* 1985; 13 : 636-44.
7. Sly SM. Urticaria and angioedema. In Berman BA, Mc Donal MD. *Differential Diagnosis and Treatment of Pediatric Allergy*. Boston, Little Brown and Co., 1981, p 427-46.
8. Champion RH, Roberts SOB, Carpenter RG, Roger JH. Urticaria and angioedema : a review of 554 patients. *Br J Derm* 1969; 81 : 588-97.
9. Sarkany I, Gaylarde PM. Negative reactions to ice in cold urticaria. *Br J Derm* 1971; 85 : 46-8.
10. Wanderer AA. Essential acquired cold urticaria. *J Allergy Clin Immunol* 1990; 85 : 531-2.
11. Wanderer AA, Grandel KE, Wasserman SI, Far RS. Clinical characteristics of cold-induced systemic reactions in acquired cold urticaria syndromes : recommendations for pervention of this complication and a proposal for diagnostic classification of cold urticaria. *J Allergy Clin Immunol* 1986; 78 : 417-23.
12. Wanderer AA, St-Pierre JP, Ellis EF. Primary acquired cold urticaria : a double blind ocmparative study of treatment with cyproheptadine, chlorpheniramine and placebo. *Arch Dermatol* 1977; 113 : 1375-7.
13. Wasserman SI. Physical urticaria and angioedema. In Lichtenstein LM, Fanci AS. *Current therapy in allergy immunology and rheumatology 1985-1986*. St. Louis, C.V. Mosby Co., 1985, p 49-51.
14. Sigler RW, Evans III R, Horakova Z, *et al.* The role of cyproheptadine in the treatment of cold urticaria. *J Allergy Clin Immunol* 1980; 66 : 309-12.