

Asthma induced by ice water ingestion in ethnic Chinese asthmatic children: a challenge

Lin Y-Z, Hsieh K-H. Asthma induced by ice water ingestion in ethnic Chinese asthmatic children: a challenge
Pediatr Allergy Immunol 1997; 8: 11–16. © Munksgaard 1996.

The purpose of this study was to investigate the relationship between ice water ingestion and the induction of asthmatic symptoms and signs in ethnic Chinese asthmatic children. Sixty asthmatic children with a positive history of exacerbation of symptoms after drinking ice water were divided randomly into two groups: 34 children were instructed to drink 250 ml of 0–4°C ice water within one minute, and 26 to drink 250 ml of 25°C warm water. All of the asthmatic children were stable when studied. Twenty-three healthy children as controls were asked to drink 250 ml of 0–4°C ice water. The three groups had forced expiratory volume in one second (FEV₁) performed at baseline and at 5, 15, 30, 60, and 90 minutes after challenge. After the spirometric test at 90 minutes the patients of the two asthmatic groups received three puffs (0.6 mg) of hexoprenaline MDI and a further spirometric test was performed 5 min after the inhalation. Cough and wheeze were monitored throughout the course of the test.

The mean FEV₁ after challenge decreased significantly only in the ice-water asthmatic group ($p=0.004$). Compared with the baseline data, the mean FEV₁ at various periods after challenge was only significantly decreased at 60 min ($p=0.035$). After hexoprenaline inhalation the FEV₁ significantly increased in the two asthmatic groups ($p<0.001$). A significant difference in FEV₁ change was noted among the three groups ($p=0.015$). Nine cases (26%) from the ice water asthmatic group, three (12%) from the warm-water asthmatic group, and none of the ice-water normal control group showed a decrease of FEV₁ greater than 15% ($p=0.018$). The greatest difference occurred between the two ice water groups. All six cases who developed symptoms after challenge, accompanied by a simultaneous decrease of FEV₁ greater than 15%, belonged to the ice-water asthmatic group. Forty-seven percent of the ice-water asthmatic group and 4% each of the two other groups had cough and/or wheeze after challenge ($p=0.0002$). In conclusion: Ice water ingestion may induce or exacerbate asthma in ethnic Chinese asthmatic children.

Abbreviation: FEV = forced expiratory volume.

Yung-Zen Lin¹, Kue-Hsiung Hsieh²

¹Department of Pediatrics, Taipei Municipal Chung Hsiao Hospital, ²Division of Allergy, Chang Gung Children's Hospital*, Taipei, Taiwan, R. O. C.

Yung-Zen Lin, Department of Pediatrics, Taipei Municipal Chung Hsiao Hospital, No. 87, Tung Teh Road, Taipei 11502, Taiwan, R. O. C.

Key words: ice water ingestion; challenge; asthma

Received August 19, 1996
Accepted November 3, 1996

A recent survey among 200 asthmatic children visiting the Paediatric Allergy Clinic of the Taipei Municipal Chung Hsiao Hospital found that 73% of the patients reported the experience of coughing or wheezing after drinking ice-cold beverages, and 88% of them had been advised by medical practitioners to refrain from ice-cold drinks. This creates a difficult situation since summer is usually rather hot and humid in subtropical Taiwan, where the average daily temperature rises above 30°C and the humidity is up to 90%, and so families find it almost impossible to prevent their asthmatic children from drinking ice-cold beverages during this season. In

1985 Wilson reported a significantly higher prevalence rate of ice-cold drinks related coughing or wheezing among Asian (63%) as opposed to non-Asian (9%) asthmatic children (1), with an increased bronchial responsiveness and a decreased FEV₁ after challenge with ice and acid in children of Asian origins (2, 3). These reports were the motivation to investigate the relationship between the ingestion of ice-cold beverages and the induction of asthma in Taiwanese patients, all of whom were of Asian origin. The prevalence rates of ice-cold drink induced asthmatic symptoms among patients here and among Asians in Wilson's report were very sim-

ilar; there was, however, no mention of any concurrent asthmatic symptoms in Wilson's provocation study during the course of the challenge. The present study was thus designed to investigate the relationship between ice water ingestion and the induction of asthmatic symptoms and signs, using spirometry and clinical symptoms as monitoring systems, and with control groups for comparison.

Patients and methods

Patients

This study included three groups. The "ice-water group" consisted of 34 asthmatic patients who were followed up at the Paediatric Allergy Clinic of the Taipei Municipal Chung Hsiao Hospital with a diagnosis of mild to moderate bronchial asthma (4) and accompanied by a positive history of ice-cold drink induced coughing or wheezing. The asthma diagnosis was based on the American Thoracic Society standards (5). Patients were eligible for study if they had no cough or wheeze audible by stethoscope examination at presentation, were at least five but under fourteen years of age, and had the ability to perform spirometry. Patients with recent respiratory tract infections were excluded. Patients who had received any aerosolized beta-agonist within six hours, or oral bronchodilators within twelve hours, before presentation, were also excluded. This group was challenged by drinking 250 ml of 0-4° C ice water (ice in water). The "warm-water group" consisted of 26 asthmatic patients who also had a positive history of ice-cold drink induced coughing or wheezing and fulfilled the same inclusion and exclusion criteria as those of the ice-water group. This group was challenged by drinking 250 ml of 25° C warm water. The "normal" group included 23 children who were physically well without recent respiratory tract disease or a past history of wheezing episodes; they all voluntarily participated in this test. This latter group received 250 ml of 0-4° C ice water. All of them were asked to drink the water within 60 seconds. The asthmatic patients were randomly divided into the two asthmatic groups according to their date of entry. The challenge was performed in an air conditioned room at an ambient temperature of 25° C in the afternoon in a summer season. Informed consents were obtained from at least one of all the subjects' parents before the study.

Measurements

Spirometry

All subjects in all three groups were well instructed how to use spirometry before the formal recording;

Table 1. demographic characteristics of the studied subjects

	Ice-water asthmatic group (n=34)	Warm-water asthmatic group (n=26)	Ice-water normal group (n=23)
Age (years)	8.82±1.90*	8.31±2.22	8.52±2.19
Range	5-12	5-14	5-13
Sex (M/F)	25/9	20/6	13/10
Severity of asthma#			
mild	5	4	
moderate	29	22	
Medications			
β ₂ -Agonists	28	22	
Theophyllin	27	22	
Inhaled steroids	4	3	
Intermittent oral steroids	10	9	
FEV ₁ (%)	91.44±13.88*	87.88±12.12	92.91±13.29
Range	62-127	57-109	78-120

*Mean±SD

#According to reference 4

their forced expiratory volume in one second (FEV₁) was performed at baseline and again at 5, 15, 30, 60, and 90 minutes after the challenge. After the spirometric test at 90 minutes, the patients of the two asthmatic groups received three puffs (0.6 mg) of a hexoprenaline metered dose inhaler through a 750 ml valved spacer; a further spirometric test was performed 5 min after this inhalation. All tests were performed using standard spirometry (Vitalograph Compact, Cat No. 42.000; Vitalograph). The FEV₁ values of at least three consecutive efforts were determined using the curve having the best FEV₁ as defined by the American Thoracic Society (6). The values were expressed as a percentage of the predicted normal values for age, height, and sex. No exercise was allowed during the course of testing.

Evaluation of clinical response

The clinical response to the ingestion challenge was monitored by asking the subjects or their accompa-

Table 2. Clinical responses to water ingestion challenge

	Ice-water asthmatic group (n=34)	Warm-water asthmatic group (n=26)	Ice-water normal group (n=23)
Coughing	9 (26%)	0	1 (4%)
Wheezing	5 (15%)	1 (4%)	0
Coughing and wheezing	2 (6%)	0	0
Total	16 (47%)*	1 (4%)*	1 (4%)*
Confidence interval	30%-64%	0%-12%	0%-12%

* p<0.00002 by Pearson chi-square test

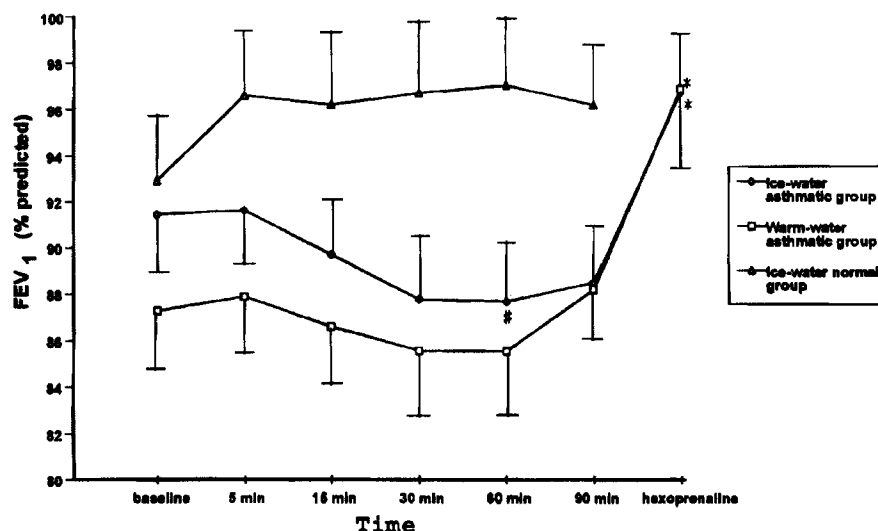


Fig. 1. The changes in FEV₁ after challenge among the three tested groups. Data are expressed as mean $\pm$ SE.

Within group analysis, $p = 0.004$ (ice-water asthmatic group). Between group analysis, $p = 0.015$ (among the three tested groups); $p = 0.001$ (between the two ice-water groups) # $p = 0.035$ when compared with the baseline value of the same group (with Bonferroni's correction); * $p < 0.001$ when compared with any other values for the same group.

nying family members whether they had had cough symptoms during the waiting periods, and by auscultating the subjects to detect any wheezing before each successive spirometric testing. This evaluation was performed by a senior pediatrician who had not been made aware of the details of this study.

Statistics

The one-way ANOVA test was used for analysis of age and baseline spirometric results. The repeated measurements of the ANOVA test were used for statistical analysis of the spirometric results before and after the water ingestion challenge for the three tested groups. Multiple comparison tests with Bonferroni's correction were used for within group statistical analysis between the baseline value and any of the five values after challenge. The χ^2 test was used for statistical analysis of sex disposition, severity of asthma, and medications, as well as the comparative frequency of the spirometric and clinical response to

the water ingestion challenge. A p value of less than 0.05 was considered statistically significant.

Results

The demographic characteristics of the three groups are shown in Table 1. There was no statistical difference with regard to age, sex or initial spirometric results among the three groups. There was no statistical difference with regard to the severity of asthma or medication categories between the two asthmatic groups.

The spirometric results before and after the water ingestion challenge are depicted in Fig. 1. Although the mean FEV₁ of the two asthmatic groups showed a decreasing trend after the challenge, only the ice-water asthmatic group was statistically significant ($p=0.004$). For within group analysis, compared with the baseline data, only the decrease in the mean FEV₁ at 60 min after challenge reached statistical significance when multiple comparison tests with Bonferroni's correction were performed

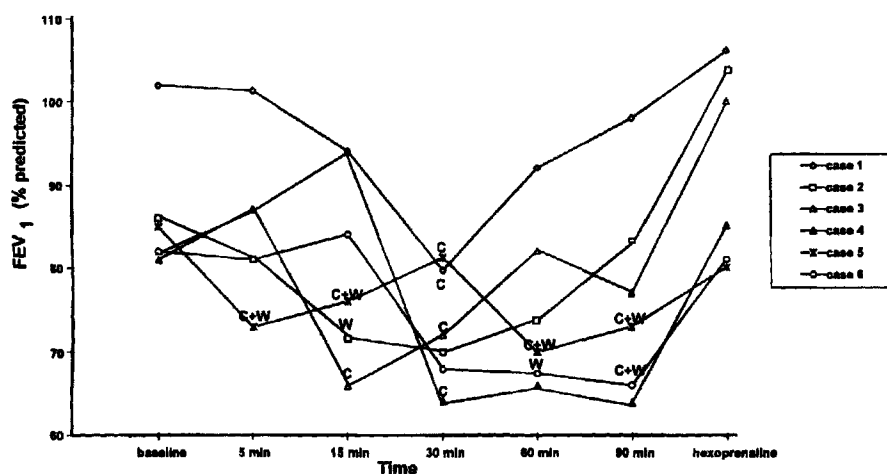


Fig. 2. The changes in FEV₁ among the six asthmatic patients who showed a decrease in FEV₁ greater than 15%, accompanied by the development of clinical symptoms. All belonged to the ice-water asthmatic group. C: coughing; W: wheezing; C+W: coughing with wheezing.

($p=0.035$). After hexoprenaline inhalation the FEV_1 significantly increased in the two asthmatic groups ($p<0.001$). On the contrary, the ice-water normal group showed a slight FEV_1 increase after challenge, but without any statistical significance. For between-group analysis, there was significant difference among all three groups after the challenge ($p=0.015$). The greatest difference occurred between the two ice-water challenge groups ($p=0.001$). Individually, nine (26%) cases of the ice-water asthmatic group, three (12%) cases of the warm-water asthmatic group, and none of the ice-water normal group had a decrease in FEV_1 of 15% or greater below the baseline ($p=0.018$). Again, the greatest difference occurred between the two ice-water challenge groups ($p=0.008$, Fisher's exact test). Nevertheless, only six cases had a decrease in FEV_1 greater than 15% accompanied by the development of symptoms (Fig.2); all six cases belonged to the ice-water asthmatic group.

The clinical response after challenge is shown in Table 2. Forty-seven percent (16/34) of the ice-water asthmatic group had coughing and/or wheezing after challenge. On the contrary, only 4% of each of the two other groups (1/26 and 1/23 respectively) had such a response ($p=0.0002$). Of the 16 cases of the ice-water asthmatic group who developed symptoms after challenge, eight (50%) had symptom onset at 5 min, five (31%) at 15 min, two (13%) at 30 min, and one (6%) at 60 min.

Discussion

The results of this study indicate that ice water ingestion in asthmatic children results in the deterioration of baseline pulmonary function and the development of clinical symptoms which are evidenced by a significant decrease in FEV_1 and a significant increase in the frequency of occurrence of clinical symptoms after challenge. To our knowledge, this study is the first study to demonstrate the development of clinical symptoms accompanied by a deterioration in pulmonary function after ice water ingestion. The clinical symptoms provoked can hardly be explained as a result of the subjects' expectation of a response to ice water ingestion, since most children would be delighted with a negative result and being allowed to take icy drinks in the hot summer season. In addition, it was almost impossible to perform the study in a double-blind model, even by administering the ice water through a naso-gastric tube, since the patients could still sense the cold feeling through the esophagus or stomach.

There have been very few reports describing asthma induced by the ingestion of ice. To the authors' knowledge, the only reports can be credited to Wilson et al., who not only surveyed asthmatic children (1) but also performed ice-ingestion challenge tests

for those with a positive history of symptoms exacerbated by ice-cold drinks (2, 3). In their first study, the symptoms induced by ice were significantly more frequent in Asian than in non-Asian children, and an increased bronchial responsiveness was induced by ice challenge but without peak expiratory flow change (2). In the later study, a significant increase in bronchial responsiveness and a maximal decrease in FEV_1 at 90 minutes following ice and acid ingestion were demonstrated in ten Asian patients, of whom, six were challenged with ice, and four with acid (3). In that study the ten patients challenged by either ice or acid were combined for assessment to determine any statistically significant changes in FEV_1 and bronchial responsiveness. The clinical symptoms of either coughing or wheezing following the challenge were not mentioned. In our study the ice water was the only agent for challenge and we demonstrated not only the more frequent clinical symptoms but also a significant decrease in FEV_1 following the challenge in the ice-water group. Although bronchial responsiveness to inhaled histamine has been shown to be more sensitive than a baseline pulmonary function test alone in detecting airway changes induced by ice (2) and by some other food substance (7, 8), nevertheless, a greater amount of ingested ice water (250 ml instead of 40 ml) and a larger number of tested subjects (34 cases) might compensate for this defect and make the test more sensitive in detecting any subtle changes. Furthermore, all of our study subjects lived in Taiwan and were of ethnic Asian origin. They were, as noted by Wilson et al., the proper candidates for the study of an ice challenge.

Using a rigid statistical assessment method (Multiple comparison tests with Bonferroni's correction), our study found a significant decrease in FEV_1 only at 60 min after challenge in the ice-water asthmatic group. On the contrary, in the study of Wilson et al. which assessed the data using a 95% confidence interval for change in FEV_1 without further correction, a small but significant fall in FEV_1 was observed at each time point, increasing to a maximum 90 min after ingestion (3). Without the Bonferroni's correction there would have been a statistically significant fall in FEV_1 occurring also at 30 min and 90 min ($p=0.027$ and $p=0.029$ respectively, Multiple comparison tests with least significant difference) after ice water challenge in the ice-water asthmatic group. In some other reports among asthmatic children, an increase in bronchial reactivity was detected 30 min after the ingestion of Pepsi-Cola (7) and tartrazine (8); a maximal fall in FEV_1 of 12% or more below the pretreatment level was detected at a mean time of 30, 20, and 5 min, respectively, after tartrazine, sodium benzoate, and sulphur dioxide challenges (9). It could not be ruled out that some

delayed type reaction might also play a role in causing ice water induced asthma, since the patients were followed for only 90 min after challenge. As a matter of fact, in a recent survey of our 200 asthmatic children, almost half of the asthmatic children with a positive history of reaction to ice-cold drinks reported that symptoms occurred 30 min or more after ingestion, among whom some also had symptoms occurring at night after daytime drinking of ice-cold drinks.

It is interesting that there was a discrepancy between the frequency of ice-induced asthmatic symptoms by questionnaire (73%), the frequency of ice-induced asthmatic symptoms by challenge (47%), the frequency of a decrease in FEV₁ greater than 15% below the baseline after challenge (26%), and the frequency of a decrease in FEV₁ greater than 15% below the baseline accompanied by simultaneous development of clinical symptoms after challenge (18%). The prevalence rate became less as the criteria set for the ice-induced asthma became more strict. The reason for this discrepancy may be that a clinical history is usually fallible, requiring further clarification; on the other hand the asthmatic response to ice water may not easily be confirmed in the laboratory. Furthermore, the response may depend on the asthmatic severity at presentation, the amount of ice water ingested, the speed and method of drinking, the water temperature, and the concurrent presence of other asthma-triggering factors such as exercise, hyperventilation, allergen exposure and upper respiratory infections. The actual situations in daily life are much more complicated than those which can be designed in a laboratory setting. Speculation here is that the real prevalence rate of ice-induced asthma should lie between 18 and 73%.

What can be learned from this study is that asthmatics are more vulnerable to ice water ingestion than normal subjects, although the mechanism for this is unclear. The difference between ice water and warm water ingestion results from a cooling of the upper gastrointestinal tract. In the study of Wilson et al.(3), there was no significant change in FEV₁ or histamine PC₂₀ after orally retained challenge with ice or acid. After the ice and acid had been swallowed, a small but statistically significant fall in FEV₁ together with a significant increase in bronchial responsiveness occurred. The esophagus was thus incriminated to be the trigger site. Bronchoconstriction after cooling of airways can indirectly result in a drop in the esophageal temperature in asthmatic subjects with postexercise asthma (10). The reverse could occur since the trachea is separated from the esophagus only by a membrane. Therefore, it may be possible that the development of clinical symptoms and fall in FEV₁

after ice water ingestion was due to the direct cooling of the upper gastrointestinal tract, including larynx, and/or the indirect cooling of the upper airway like trachea. Another possible mechanism may be similar to the association between gastroesophageal reflux and asthma, which has been reported by many authors (11–13). The major cause of gastroesophageal reflux induced asthma has been reported to be a reflex-mediated bronchospasm from stimulation of the esophagus without direct aspiration (11, 12), which can be blocked by topical lidocaine anesthesia of the distal esophagus in awake asthmatic subjects (11). Both mechanisms still need to be proven.

For a long time in this ethnic Chinese culture it has been taken for granted by practitioners and parents who take care of asthmatic children that ice-cold drinks usually exacerbate asthmatic symptoms. The people living here always warm-feed their babies, either learning from their own experience or through advice, not to take cold drinks when wheezing or coughing, and usually drink cold beverages only on summer days. This custom differs greatly from that of most Caucasian people who feed their children cold drinks early and throughout the four seasons. The speculation is that this habit may be one of the reasons for the greater sensitivity of Asian asthmatic children to ice-induced asthma. Needless to say, racial differences may be another reason.

In conclusion, ice water ingestion may induce or exacerbate asthma in ethnic Chinese asthmatic children, but the mechanism involved still needs further study.

Acknowledgements

The authors express their thanks to Wan-Hui Chang of the Epidemiology Section of Public Health, the Medical College of National Taiwan University, for her great help in statistical assistance, and to Drs. Min-Ching Chen, Ching Jong Shyu and Chun-Po Lin of the Pediatric Department, Taipei Municipal Chung Hsiao Hospital, for their technical assistance.

References

1. WILSON NM. Food related asthma: a difference between two ethnic groups. *Arch Dis Child* 1985; 60: 861–5.
2. WILSON NM, DIXON C, SILVERMAN M. Increased bronchial responsiveness caused by ingestion of ice. *Eur J Respir Dis* 1985; 66: 25–30.
3. WILSON NM, CHUDRY N, SILVERMAN M. Role of the oesophagus in asthma induced by the ingestion of ice and acid. *Thorax* 1987; 42: 506–10.
4. ELLIS EF. Asthma in infancy and childhood. In: MIDDLETON E JR, REED CE, ELLIS EF, ADKINSON NF JR, YUNGINGER JW, BUSSE WW. eds. *Allergy, principles and practice*, 4th ed. St. Louis, Missouri: Mosby-Year Book, Inc., 1993: 1225–62.

5. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. *Am Rev Respir Dis* 1987; 136: 225-44.
6. American Thoracic Society. Standardization of spirometry --- 1987 update. *Am Rev Respir Dis* 1987; 136: 1285-98.
7. WILSON N, VICKERS S, TAYLOR G, SILVERMAN M. Objective test for food sensitivity in asthmatic children: increased bronchial reactivity after cola drinks. *Br Med J* 1982; 284: 1226-8.
8. HARIPARSAD D, WILSON N, DIXON C, SILVERMAN M. Oral tartrazine challenge in childhood asthma: effect on bronchial reactivity. *Clin Allergy* 1984; 14: 81-5.
9. FREEDMAN BJ. Asthma induced by sulphur dioxide, benzoate and tartrazine contained in orange drinks. *Clin Allergy* 1977; 7: 407-15.
10. DEAL EC, MCFADDEN ER, INGRAM RH, JAEGER JJ. Esophageal temperature during exercise in asthmatic and non-asthmatic subjects. *J Appl Physics* 1979; 46: 484-90.
11. MANSFIELD LE, STEIN MR. Gastroesophageal reflux and asthma: a possible reflex mechanism. *Ann Allergy* 1978; 41: 224-6.
12. DAVIS RS, LARSON GL, GRUNSTEIN MM. Respiratory response to intraesophageal acid infusion in asthmatic children during sleep. *J Allergy Clin Immunol* 1983; 72: 393-8.
13. GOODALL RJR, EARIS JE, COOPER DN, BERNSTEIN A, TEMPLE JG. Relationship between asthma and gastroesophageal reflux. *Thorax* 1981; 36: 116-21.
14. BABB RR, NOTRANGELO J, SMITH VM. Wheezing, a clue to gastroesophageal reflux. *Am J Gastroenterol* 1970; 53: 230-2.