

THE EFFECT OF FRESH ORANGE JUICE ON BRONCHIAL HYPERREACTIVITY IN ASTHMATIC SUBJECTS

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ABSTRACT

We studied 16 mild stable asthmatic subjects to determine if orange juice increases nonspecific bronchial hyperreactivity (NSBH). In 9 subjects, bronchial responsiveness to histamine was assessed before and after water ingestion on the control day, and orange ingestion on a consecutive day. The mean (\pm SD) ratio of \log_{10} PD₂₀ FEV₁ after water: \log_{10} PD₂₀ FEV₁ before water (1.00 ± 0.13) was not significantly different from the mean (\pm SD) ratio of \log_{10} PD₂₀ FEV₁ after orange: \log_{10} PD₂₀ FEV₁ before orange (0.97 ± 0.12). To avoid the possibility of histamine tachyphylaxis, 7 subjects participated in a second protocol in which histamine PD₂₀ FEV₁ was determined on a control day (geometric mean 0.11 mg.) and again two days later, thirty minutes after ingestion of orange juice (geometric mean 0.06 mg). There was no significant difference in the PD₂₀ FEV₁ ($p = 0.344$). Our data show that ingestion of fresh orange juice per se did not heighten NSBH in our subjects. (PD₂₀ FEV₁ is the dose of histamine required to produce a twenty percent fall in forced expiratory volume in one second [FEV₁]).

Keywords: Fresh orange juice, bronchial hyperreactivity, asthmatics.

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INTRODUCTION

Dietary indiscretion can lead to asthmatic attacks in some asthmatic subjects. Several substances like nuts, eggs, milk, chocolate, fish as well as food additives such as sulphur dioxide, benzoate and tartrazine can cause wheezing in asthmatic subjects (1,2). In our clinic, we found that many of our asthmatic subjects avoid orange drinks either because they developed symptoms of cough or they had been told that orange drinks can aggravate their asthma. Bronchial responsiveness has been shown to correlate with the severity of bronchial asthma. This study was carried out to see if freshly prepared orange juice can cause an increase in NSBH.

PATIENTS AND METHODS

Sixteen mild stable asthmatics were selected on the basis of willingness to participate in the study, from the chest clinic of Tan Tock Seng Hospital. They were free

of any form of respiratory tract infection for at least six weeks before the study and were on salbutamol tablet or inhaler only when necessary. They were also not on any medicine for at least two weeks preceding the study. All were non-smokers.

Nine subjects (8 males) with a mean (\pm SD) age of 24.9 ± 7.0 years (Table I) participated in the first protocol in which they attended the laboratory on two consecutive days and at the same time each day. They were instructed not to eat or drink 8 hours before the study. On arrival at the laboratory, the subjects were rested for 10 minutes and then their baseline FEV₁s were recorded with a Spiro Analyzer ST-100. A histamine inhalation test (HIT) was then performed. The patients were rested until their FEV₁s returned to $\pm 5\%$ of the baseline before they took 250 ml of water warmed to 37°C. Thirty minutes later, they performed a second HIT. On the second day, the test was carried out at the same time of the day and the

TABLE I.
DETAILS OF SUBJECTS IN PROTOCOL 1

| Subject | Sex | Age(yr) | Baseline FEV ₁ (l) |
|---------------|-----|--------------|-------------------------------|
| 1 | F | 16 | 2.20 |
| 2 | M | 21 | 2.33 |
| 3 | M | 30 | 3.71 |
| 4 | M | 25 | 3.08 |
| 5 | M | 39 | 3.01 |
| 6* | M | 25 | 2.78 |
| 7* | M | 24 | 3.27 |
| 8 | M | 17 | 3.46 |
| 9* | M | 27 | 3.19 |
| Mean \pm SD | | 24 \pm 7.0 | 3.00 \pm 0.50 |

* Develop cough after taking orange drink

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protocol was identical except that freshly prepared orange juice with a pH of 2.5 to 3 was used instead of water.

Seven subjects (6 males) with a mean (\pm SD) age of 30.6 ± 10.2 years (Table II) took part in a second protocol which was designed to avoid possible histamine tachyphylaxis. After baseline FEV₁s were determined, the subjects performed a HIT on the first day. The subjects then returned 2 days later and at the same time of day. Once the baseline FEV₁s were determined, they ingested 250 ml of freshly prepared orange juice warmed to 37°C and 30 minutes later performed the HIT.

TABLE II.
DETAILS OF SUBJECTS IN PROTOCOL 2

| Subject | Sex | Age(yr) | Baseline FEV ₁ (l) |
|---------------|-----|-----------------|-------------------------------|
| 1 | M | 26 | 3.62 |
| 2 | M | 20 | 3.48 |
| 3 | M | 17 | 3.70 |
| 4 | F | 35 | 1.98 |
| 5 | M | 32 | 2.65 |
| 6* | M | 39 | 2.56 |
| 7* | M | 45 | 2.37 |
| Mean \pm SD | | 30.6 ± 10.2 | 2.91 ± 0.68 |

* Develop cough after taking orange drink

HIT was performed only when the subject's baseline FEV₁ was not less than 80% of his predicted. This test was carried out using the Mefar Dosimeter MB 3. This method required two strengths of histamine, 0.1% and 1%, in addition to the 0.9% normal saline control. The inhalation time was set at 1.2 seconds followed by a pause of 6 seconds. The subjects first inhaled 5 puffs of saline and then had their control FEV₁s determined one minute later. They then inhaled varying puffs of 0.1% and then 1% histamine solutions to obtain the cumulated doses (mg) as shown in Table III. Their FEV₁s were measured one minute after each serial dose of histamine. The inhalations were stopped when their resulting FEV₁s were equal to or less than 80% from their control FEV₁s. A dose response curve was constructed and the dose

that caused a 20% fall in FEV₁ (PD₂₀ FEV₁) was calculated by linear interpolation after logarithmic conversion.

Differences in mean FEV₁ and PD₂₀ FEV₁ were assessed by Wilcoxon Signed Rank Test. Comparisons of PD₂₀ FEV₁ were performed after logarithmic transformation.

RESULTS

First Protocol

The mean (\pm SD) baseline FEV₁ remained stable in the two study days before all 4 HIT: before first HIT 3.00 ± 0.5 l (water), 2.88 ± 0.68 l (orange); before second HIT 3.01 ± 0.6 l (water), 3.00 ± 0.59 l (orange). Both water and orange did not change histamine PD₂₀ FEV₁ significantly (Table IV). When the two ratios of log₁₀ PD₂₀ FEV₁ after and before each test drink were compared, no significant difference were found (Fig 1), the mean (\pm SD) ratio for control day was $1.00 (\pm 0.13)$ as compared to second (orange) day of $0.97 (\pm 0.12)$.

TABLE IV.
HISTAMINE PD₂₀ FEV₁ (MG) BEFORE AND 30 MINUTES AFTER EACH TEST DRINK IN PROTOCOL 1

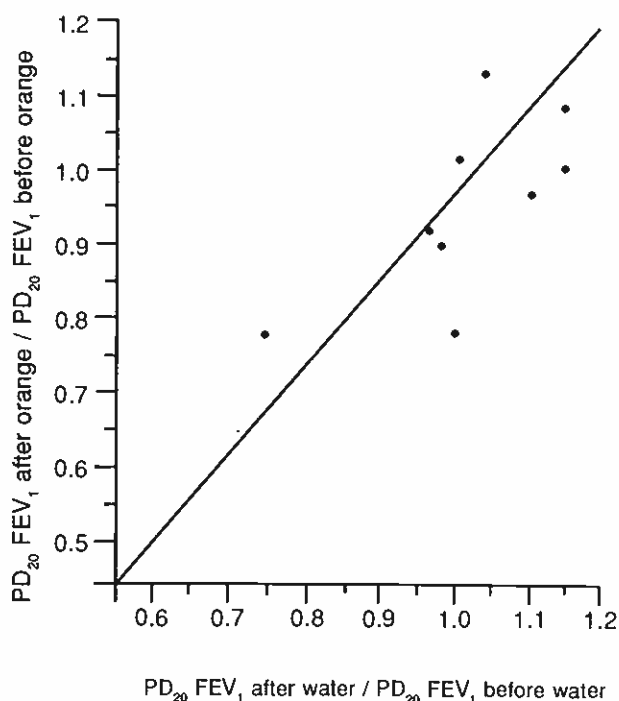
| Subject | Water | | Orange | |
|----------------|--------|-------|--------|-------|
| | Before | After | Before | After |
| 1 | 0.16 | 0.36 | 0.21 | 0.23 |
| 2 | 0.09 | 0.08 | 0.09 | 0.07 |
| 3 | 0.52 | 0.97 | 0.43 | 0.39 |
| 4 | 0.51 | 0.49 | 1.12 | 0.25 |
| 5 | 0.79 | 2.18 | 0.33 | 0.60 |
| 6 | 0.09 | 0.03 | 0.10 | 0.04 |
| 7 | 0.52 | 0.49 | 0.42 | 0.49 |
| 8 | 0.15 | 0.11 | 0.30 | 0.21 |
| 9 | 1.12 | 1.23 | 0.87 | 2.23 |
| Geometric Mean | 0.31 | 0.33 | 0.32 | 0.27 |

TABLE III.
TABLE SHOWING NUMBER OF PUFFS OF EACH HISTAMINE SOLUTION TO OBTAIN THE CUMULATIVE DOSES

| | NORMAL SALINE (0.9%) | HISTAMINE SOLUTION | | | | | | | | | |
|-----------------------|----------------------|--------------------|-----|-----|-----|----|---------------|----|-----|-----|--|
| | | 1 mg/ml(0.1%) | | | | | 10 mg/ml (1%) | | | | |
| Serial number of dose | control | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | |
| Number of puffs | 5 | 1 | 1 | 2 | 2 | 4 | 1 | 1 | 3 | 6 | |
| Cumulative dose (mg) | | .02 | .04 | .08 | .12 | .2 | .4 | .6 | 1.2 | 2.4 | |

Fig. 1

PD₂₀ FEV₁ after orange/PD₂₀ FEV₁ before orange Vs PD₂₀ FEV₁ after water/PD₂₀ FEV₁ before water



Second Protocol

The mean (\pm SD) baseline FEV₁ on the first and second day (2.91(\pm 0.68) l and 2.88(\pm 0.69) l respectively) were not significantly different and did not change after taking fresh orange juice (2.92(\pm 0.74) l).

Fresh orange juice did not significantly change the histamine PD₂₀FEV₁ (p=0.37) (Table V).

TABLE V.
HISTAMINE PD₂₀ FEV₁ (MG) ON DAY 1
AND DAY 2 IN PROTOCOL 2

| Subject | Day 1 | Day 2 (After orange) |
|----------------|-------|----------------------|
| 1 | 0.06 | 0.03 |
| 2 | 1.03 | 0.62 |
| 3 | 0.15 | 0.07 |
| 4 | 0.10 | 0.06 |
| 5 | 0.02 | 0.02 |
| 6 | 0.29 | 0.18 |
| 7 | 0.03 | 0.01 |
| Geometric Mean | 0.11 | 0.06 |

DISCUSSION

Based on the results of our study, we have not found that fresh orange juice increases NSBH. We used warm orange juice to eliminate the effect of temperature as the studies by Wilson et al found that ice water ingestion caused a change in NSBH (3,4). The similar baseline FEV₁ values at all HITs (in protocols 1 and 2) confirmed the clinical stability of the asthmatic subjects and allowed comparisons of histamine PD₂₀FEV₁ to be made.

NSBH exhibits a circadian rhythm (5-7). In both protocols, the HITs were performed at the same time of day on the control and study days, thus allowing for circadian variation. Only 2 of the subjects were females, and thus any menstrual cyclical effects on NSBH (8,9) would not substantially affect our results.

In protocol 1, the choice of using water in the control day may not be ideal, as the subject can obviously

differentiate water from fresh orange juice. However we chose not to blind the patient, as it would require oesophageal intubation with a Ryle's tube.

Manning et al showed that mild asthmatics exhibit histamine tachyphylaxis even at 6 hours, when repeatedly challenged to inhaled histamine. They found that the effect had completely worn off at 48 hours (10). We therefore devised protocol 2 to overcome the possible effect of histamine tachyphylaxis on PD₂₀FEV₁.

In conclusion, we found that orange per se has no effect on NSBH in our subjects.

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