Angina pectoris during inhalation of cold air

Reactions to exercise

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SUMMARY Twelve male patients, with effort angina and a history of cold intolerance, performed brief submaximal exercise bicycle tests with separation of inspiratory and room air. In one test, the patients exercised in a normal room (20°C), breathing either normal or very cold air (-35°C). In another test, environmental air was either normal or -10°C, and four combinations of inspiratory and room air were used: 20/20°C, -10/20°C, 20/-10°C, and -10/-10°C.

Inhalation of very cold air (-35°C) caused a significant decrease in maximal workload. Heart rate, systolic blood pressure, and rate-pressure product were significantly higher during exercise when compared with findings in the normal room. The decrease in maximal workload correlated significantly with the increase in heart rate and rate-pressure product during exercise. In five patients, the decrease in maximal workload exceeded 5 per cent. In contrast, inhalation of moderately cold air (-10°C) did not cause any significant changes in maximal workload or non-invasive variables. The decrease in maximal workload exceeded 5 per cent in one patient. Exposure to a cold room (-10°C), with inhalation of normal air, caused changes in maximal workload, heart rate, and blood pressure similar to those caused by inhalation of very cold air. Six patients showed a decrease in maximal workload exceeding 5 per cent.

In conclusion, skin cooling seems to be far more important in its effects on heart load and the working capacity in patients with effort angina than cold air inhalation in a moderately cold environment; inhalation of very cold air, however, does cause changes in working capacity and non-invasive variables similar to those of exposure to a cold environment. Increase in heart work during exercise is likely to cause the decrease in working capacity observed both with skin cooling and cold air inhalation.

Exposure to cold often causes a worsening of effort angina. In a previous investigation¹ we found that the decrease in work capacity in a cold environment was related to an increase in both heart rate and systolic blood pressure during exercise in the cold as compared with a normal environment. The relative importance of skin and airway cooling was not studied. The results of other investigations suggest that local cooling of the skin leads to an increase in heart work resulting from an increase in peripheral vascular resistance.² Reports on cold air inhalation have given conflicting evidence, both in studies at rest³ and during atrial pacing.⁴ To our knowledge there are no reports on the effects of breathing cold air at a normal room temperature on effort angina.

The aims of this investigation were to study the effects of cold air inhalation on patients with effort

angina, at rest, during, and after exercise, and to correlate the changes in work capacity with changes in heart rate, blood pressure, and ST depression on the electrocardiogram. Studies were also carried out to determine whether the effects of cold air inhalation were different in normal and in cold environments.

Subjects

Twelve male patients with a history of cold intolerance (all non-smokers, mean age 51 years, range 45 to 60) were invited to participate. All gave informed consent to the study, which had been approved by the Ethical Committee of the Medical Faculty. All patients had a history of stable angina pectoris for at least 12 months. Six patients had had one or more myocardial infarctions. All had exercise-induced angina and 0.2 to 0.6 mV depres-

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sion of horizontal or downsloping ST segments on the electrocardiogram at the end of exercise. On a standardised stepwise ergometer test their work capacity, expressed as $W_{\max}$ 6 min⁵ was on the average 100 W (range 70 to 150). In all patients this was limited by angina. None had hypertension, but one patient had symptoms and signs of chronic bronchitis. Six patients used beta-adrenergic receptor blocking agents in constant dosage, but no other treatment except short-acting glyceryl trinitrate was allowed.

Methods

ENVIRONMENT

Observations were made both in a cold environment in a special chamber and at normal room temperature. In order to separate the temperature of the environment from that of the inspired air, the patients breathed through a mouthpiece (dead space 15 ml) connected to an open pipe, 8 cm wide with suction at one end (Fig. 1) producing a slight negative pressure (0.1 kPa) at the mouth at end-expiration. Valves were not used, as they caused warming of the inspired air (5 to 15°C) (unpublished observations). Environmental temperatures were kept at $20 \pm 1^\circ\text{C}$ (SD), with no wind and a relative humidity of 40 ± 8 per cent, or at $-10 \pm 0.4^\circ\text{C}$, with wind directed toward the face and trunk at a velocity of 2.2 ± 0.1 m/s and an estimated relative humidity of 75 per cent. Temperatures of inspired air, measured 6 cm from the mouthpiece, were $20 \pm 0.2^\circ\text{C}$, $-10 \pm 0.1^\circ\text{C}$, and $-35 \pm 0.2^\circ\text{C}$. Temperature was measured with a copper/constantan thermocouple, wind velocity with a warm-wire anemometer, and relative humidity with a hair hygrometer.

In the room at normal temperature the patients were dressed in normal indoor clothing. In the cold chamber standardised clothing was added. The mean skin temperature was found to fall by 5.2°C during exercise in the cold environment (-10°C , 2.2 m/s). (For details, see Lassvik and Areskog.¹)

To obtain an estimate of the temperature changes in the airway, a very thin thermocouple (diameter 0.03 mm) was placed in the centre of the mouthpiece, 1 cm from the mouth. The mouthpiece was connected to a heated pneumotachograph and flow was integrated to volume. Temperature and volume of expiratory air were recorded on a high-frequency response X-Y recorder. The pneumotachograph was calibrated with known volumes. Two patients expired into the mouthpiece, immediately after inspiration of cold air ($-10 \pm 0.1^\circ\text{C}$), at various respiratory rates, tidal volumes and forces of

expiration. Thermocouples of this size have been shown to give true values of respiratory air temperature within wide ranges of air temperature and flow.⁶

TEST PROCEDURE

Two test situations were used. In the first, the patients exercised in a normal room, breathing either air at 20°C or very cold air at -35°C . Thus two conditions were obtained, temperatures of respiratory and room air being 20 and 20°C , respectively, or -35 and 20°C . The order of the tests was randomised and an initial trial test in the normal room was always performed, making a total of three exercise tests at each session.

In the second test, the patients exercised both in a normal room and in a cold room (-10°C), breathing either normal air or moderately cold air (-10°C). Thus four conditions were obtained, respiratory and room air temperatures being in turn 20 and 20°C , respectively, -10 and 20°C , 20 and -10°C , and -10 and -10°C (Fig. 1). The order of the tests was randomised and the tests were performed on a second day in reversed order. An initial trial exercise test was performed; thus, in all five serial exercise tests were performed at each session.

Exercise tests were performed in the sitting position on a bicycle ergometer (Siemens-Elema 380), with an initial load of 50 W increasing by 10 to 30 W per minute. Moderately severe angina was set as the endpoint of exercise, with a total exercise time of four to eight minutes. A six lead precordial electrocardiogram (CH leads, with a forehead reference electrode) was recorded continuously at a paper speed of 10 mm/s. ST depression was measured at appearance of angina and at maximal workload from recordings at a paper speed of 50 mm/s. Heart rate was calculated from the recordings, and systolic blood pressure was measured by the cuff method. (For further details, see Lassvik and Areskog.¹)

The patients, sitting on the bicycle at ambient temperature, were connected to the mouthpiece, from five minutes before to four minutes after exercise. Heart rate and blood pressure were measured after five minutes sitting on the bicycle before exercise, every minute during exercise, just before stopping, and every minute for four minutes after exercise. The rate-pressure product (heart rate $\times$ systolic blood pressure) was calculated. Peak expiratory flow was measured with a Wright peak flow meter, 4.5 minutes after exercise. Rest intervals between tests were 30 minutes. During this time the patients were allowed to move around freely in a normal environment. During exercise the work-

load at appearance of pain and the maximal workload were noted. Measurements were also made during exercise at three minutes, when most of the patients had no pain, and at approximately 4.5 minutes, when all patients had angina. After exercise, the time for disappearance of pain was noted.

All tests were performed at the same time of day for each patient. Patients were not allowed to take food, nitrites, or muscular exercise for two hours before the tests. All patients had previously performed five serial exercise tests at normal temperature to establish reproducibility.⁷

STATISTICS

For each patient the mean values of the two sets of

randomised exercises were calculated and evaluated using Student's *t* test for paired observations, and with regression analyses.⁸

Results

Inhalation of very cold air (-35°C) caused a significant decrease in the patients' work capacity, expressed as workload at appearance of pain and maximal workload, by 5 ± 1 per cent (mean $\pm$ SEM) ($p < 0.01$) (Table 1). The decrease in maximal workload exceeded 5 per cent in five patients (Fig. 2). *Inhalation of moderately cold air* (-10°C) did not cause any decrease in either workload at appearance

Fig. 1 Separation of inhaled and environmental air. In another situation the patients breathed very cold air (-35°C).

Table 1 Work capacity, ST depression during exercise, and peak expiratory flow: values in normal room and changes in cold conditions

	Temperatures* (inhaled air/room)				
	N/N (control)	$-35^{\circ}\text{C}/\text{N}$ (absolute changes)	N/N (control)	$-10^{\circ}\text{C}/\text{N}$ (absolute changes)	$\text{N}/-10^{\circ}\text{C}$ (absolute changes)
Workload at appearance of pain (W)	122 $\pm$ 9	-7 $\pm$ 2†	119 $\pm$ 9	-1 $\pm$ 2	-8 $\pm$ 2‡
Maximal workload (W)	146 $\pm$ 10	-7 $\pm$ 2†	142 $\pm$ 11	-1 $\pm$ 1	-7 $\pm$ 2‡
Time for disappearance of pain (s)	126 $\pm$ 26	46 $\pm$ 34	118 $\pm$ 21	3 $\pm$ 35	-12 $\pm$ 28
ST depression at appearance of pain (mV $\times$ 10)	1.6 $\pm$ 0.3	0.1 $\pm$ 0.1	1.5 $\pm$ 0.3	0 $\pm$ 0	0.4 $\pm$ 0.2
ST depression at maximal workload (mV $\times$ 10)	2.5 $\pm$ 0.3	0 $\pm$ 0	2.6 $\pm$ 0.3	0 $\pm$ 0	0.1 $\pm$ 0
Peak expiratory flow (l/min)	494 $\pm$ 32	4 $\pm$ 3	495 $\pm$ 32	4 $\pm$ 3	7 $\pm$ 4

Mean values $\pm$ SEM.

* N = 20°C . † $p < 0.01$. ‡ $p < 0.001$.

of pain or maximal workload ($1 \pm 0\%$) (Table 1) regardless of room temperature. The decrease in maximal workload exceeded 5 per cent in only one patient (Fig. 2). Exposure to cold (-10°C) with inhalation of normal air caused a significant decrease in workload at appearance of pain ($7 \pm 1\%$) ($p < 0.001$) (Table 1) and maximal workload ($5 \pm 1\%$) ($p < 0.001$) (Table 1), and the decrease of maximal workload exceeded 5 per cent in six patients (Fig. 2). In one patient very cold air inhalation caused a much greater decrease in maximal workload than exposure to the cold room (16% and 2%, respectively); otherwise differences between the two conditions were small.

Time for disappearance of pain, ST depression at appearance of pain and maximal workload, and peak expiratory flow values did not differ between any of the situations compared (Table 1). Several patients had occasional unifocal premature ventricular beats in the normal room, and the frequency of these did not increase on exposure to cold.

At rest, blood pressure and rate-pressure product were significantly higher ($p < 0.01$) (Table 2) in the cold room than in the normal room. During exercise, heart rate, blood pressure and rate-pressure product were significantly higher both on inhalation of very cold air ($p < 0.05$ for all variables) and in the cold room ($p < 0.05$, $p < 0.001$, and $p < 0.01$,

respectively). At maximal workload, blood pressure was significantly higher ($p < 0.05$) in the cold room, whereas heart rate and rate-pressure product were unchanged compared with the normal room. After exercise, inhalation of very cold air was followed by significantly higher blood pressure at two and four minutes ($p < 0.05$) and higher rate-pressure product at two minutes ($p < 0.05$). Heart rate was significantly lower ($p < 0.01$) in the cold room and blood pressure higher ($p < 0.001$) two and four minutes after exercise, and rate-pressure product higher at four minutes ($p < 0.01$). Inhalation of moderately cold air did not cause any changes in heart rate, blood pressure, or rate-pressure product at rest, during, or after exercise (Table 2).

During inhalation of very cold air, a significant correlation was found between the decrease in maximal workload and the increase in heart rate and rate-pressure product at three minutes' exercise ($p < 0.05$ and $p < 0.01$, respectively) (Fig. 3), and the increase of rate pressure product at 4.5 minutes ($p < 0.05$). Likewise, in the cold room with inhalation of normal air, there was a significant correlation between decrease in maximal workload and increase in heart rate and rate-pressure product both at three and 4.5 minutes ($p < 0.01$ and $p < 0.001$, respectively).

Temperature of expired air after inhalation of

Fig. 2 Changes in maximal workload (MWL) during inhalation of very cold air (left), during inhalation of cold air (middle), and on exposure to cold with inhalation of normal air (right). Bars show mean values $\pm$ SEM.

cold air (-10°C): both on moderate and forced breathing (respiration rate 20/min and 42/min, respectively, and tidal volumes 1.2 and 1.7 litres, respectively) temperature increased from $-5 \pm 0.1^{\circ}\text{C}$ to 25°C within the first 100 ml of expiration and to 30°C within 200 ml (calculated as a mean of five consecutive breaths). During single breaths, with maximal force of expiration, temperature increased from $-5.8 \pm 0.2^{\circ}\text{C}$ to 25°C within the first 150 ml of expiration. The end-expiratory temperature was always $32 \pm 0.1^{\circ}\text{C}$. Measured dead space of the mouth was 70 ml.

Discussion

Inhalation of very cold air (-35°C) caused a significant decrease in work capacity in a group of patients with effort angina, all of whom gave a history of cold intolerance. In contrast, no changes in maximal workload were seen during inhalation of moderately cold air (-10°C), whether the environment was normal or cold. When the patients were exposed to a cold environment (-10°C) with inhalation of normal air, a significant decrease

Table 2 Heart rate, systolic blood pressure, and rate-pressure product at rest, during, and after exercise

Temperatures* (N=20°C) (inhaled air/room)					
	N/N (control)	-35°C/N (absolute changes)	N/N (control)	-10°C/N (absolute changes)	N/10°C
Heart rate (beats/min)					
Rest	71 ± 4	2 ± 2	73 ± 3	-2 ± 1	1 ± 2
Exercise 3 min	108 ± 4	2 ± 1*	110 ± 6	1 ± 1	3 ± 1*
4.5 min	125 ± 7	2 ± 1*	127 ± 7	0 ± 1	3 ± 1*
Maximal workload	131 ± 7	-1 ± 1	133 ± 7	-1 ± 1	-1 ± 1
Recovery 2 min	80 ± 6	-2 ± 1	82 ± 6	-1 ± 2	-6 ± 2†
4 min	76 ± 5	-2 ± 3	77 ± 5	-1 ± 1	-4 ± 1†
Systolic blood pressure (mmHg)					
Rest	123 ± 5	6 ± 3	127 ± 6	0 ± 2	13 ± 4†
Exercise 3 min	156 ± 6	4 ± 3*	155 ± 8	0 ± 1	9 ± 2‡
4.5 min	163 ± 6	3 ± 3*	165 ± 8	0 ± 1	7 ± 1‡
Maximal workload	167 ± 7	3 ± 3	171 ± 8	-1 ± 1	3 ± 2*
Recovery 2 min	147 ± 5	13 ± 4*	154 ± 6	4 ± 3	21 ± 4‡
4 min	129 ± 4	10 ± 3*	141 ± 5	0 ± 2	22 ± 4‡
Rate pressure product (units × 10⁻³)					
Rest	88 ± 7	7 ± 2	94 ± 8	-3 ± 3	13 ± 4‡
Exercise 3 min	169 ± 14	7 ± 3*	171 ± 17	1 ± 3	13 ± 4†
4.5 min	203 ± 14	5 ± 3*	209 ± 17	0 ± 3	9 ± 3†
Maximal workload	220 ± 17	1 ± 5	227 ± 19	-2 ± 2	2 ± 2
Recovery 2 min	118 ± 13	8 ± 4*	176 ± 13	1 ± 4	7 ± 5
4 min	99 ± 9	5 ± 4	109 ± 10	-2 ± 3	10 ± 3†

Mean values ± SEM.

* p < 0.05. † p < 0.01. ‡ p < 0.001.

Fig. 3 Correlation between changes of maximal workload (MWL), and changes in heart rate (HR), systolic blood pressure (BP), and rate-pressure product (RPP) during exercise (3 min) during inhalation of very cold air (-35°C).

in maximal workload occurred, comparable to that found on inhalation of very cold air.

Thus it seems that though cooling of the airways may cause a decrease in work capacity in patients with angina, lower inhaled air temperatures are needed to reduce work capacity as much as with cooling the clothed body. One reason for this might be that heat losses via the airways are small compared with those via the skin, amounting to between 10 and 20 per cent of total heat loss.⁹ The resulting fall in temperature in the lungs and the pulmonary venous blood is likely to be small, probably less than 0.2°C in the conditions used in this study (heat losses calculated according to Fanger¹⁰). Furthermore, our observations and those of others⁹⁻¹¹ indicate that cold air does not reach the alveoli in normal lungs, because inspired air is warmed in the upper airways. Since the venous blood from the upper airways returns to the right heart, cooled blood may never reach the left heart and the coronary arteries. The observations of Leon *et al.*³ support this assumption, as only slight temperature changes were found in the left atrium, during inhalation of cold air (below -20°C) at rest.

During inhalation of very cold air, in this investigation, heart rate, systolic blood pressure, and rate-pressure product increased significantly during exercise, and a significant correlation was found between the decrease in maximal workload and the increase in heart rate and rate-pressure product. Since rate-pressure product at maximal load was not different in normal and cold situations, the increase of rate-pressure product at submaximal load probably reflects an increase in myocardial oxygen demand.¹² Thus, the decrease in work capacity during inhalation of very cold air is likely to have been caused by an increase in myocardial oxygen demand resulting from the increase in heart rate and blood pressure during exercise.

The cold-induced increases in heart rate, blood pressure, and rate-pressure product during exercise were similar on inhalation of very cold air and on exposure to a cold environment with inhalation of normal air, suggesting that the haemodynamic changes have the same cause. A further indication of this is that both with cold air inhalation and with exposure to cold, blood pressure was significantly higher after exercise than in normal conditions. Skin cooling is known to cause an increase in peripheral resistance and blood pressure as a result of stimulation of cold receptors and an increase in the sympathetic outflow to the skin vessels.¹³⁻¹⁴ As cold receptors are situated not only in the skin but also in the mucous membranes of the airways, notably in the nose and tongue,¹⁵ stimulation of cold receptors is likely to occur also

with cold air inhalation. Since the cooled surface is smaller in the airways than in the skin, and cooling occurs mainly during inspiration, the total stimulation of cold receptors is probably less with cold air inhalation. This might explain why colder air is needed to produce the same changes in blood pressure during inhalation of cold air as with skin cooling.

Another interesting observation in this investigation was that cold caused greater increase in heart rate during exercise, in spite of a very short exposure to cold before exercise (five minutes). This indicates a reflex cause of the heart rate increase and confirms the observations of other investigators,¹⁶ who found that exposure to an ice-cold shower was followed by an increase in heart rate and cardiac output within seconds. Thus, cold exposure probably causes an increase in the work of the heart not only because of an increase in afterload but also because of an increase in heart rate.

Other possible effects of exposure to cold are increase in left ventricular contractility,³ increase in left ventricular end-diastolic pressure,² and increase in the cellular metabolism, caused by release of catecholamines.¹⁷ Furthermore, Hattenhauer and Neill,⁴ using atrial pacing, found signs and symptoms of myocardial ischaemia on cold air inhalation, at levels of heart rate and blood pressure well below those found during angina at normal temperature. As this could not be explained by left ventricular pressure changes, blood pH changes, or coronary angiographic changes, they suggested that spasm of minute coronary vessels caused the ischaemia. This possibility is also suggested by the findings of Mudge *et al.*¹⁸ who noted decreased coronary blood flow during the cold pressor test, despite an increase in arterial blood pressure, in patients with coronary disease.

In conclusion, general skin cooling or inhalation of very cold air caused a decrease in the work capacity in about half of the patients investigated; this could be explained by a higher myocardial oxygen demand than during exercise at a normal temperature. With cold air inhalation compared with skin cooling, however, lower temperatures are needed to produce similar reduction in work capacity.

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