Medicina Sportiva
Med Sport 14 (2): 50-55, 2010
DOI: 10.2478/v10036-010-0010-9

THE SUSTAINED EFFECT OF NASAL INSUFFLATIONS ON CARDIO-RESPIRATORY, METABOLIC AND PERFORMANCE MEASURES IN ATHLETES UNDER RESPIRATORY STRESS

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Abstract

Introduction: Whilst there are many studies of the benefits of non-invasive respiratory support in cardiovascular and respiratory compromised individuals during the insufflation period, little is known on what effects, if any, remain following the insufflation.

Aim of study: The present study was carried out to investigate the effects of nasal insufflation on various physiological variables and exercise performance in a group of male endurance athletes under respiratory stress.

Materials and methods: Eight male competitive endurance athletes (30 ± 6 yr, $\dot{V}O_2$max: 65 ± 8 ml kg^{-1} min^{-1}) were exposed for 30 minutes to: i) 25 L min^{-1} nasal insufflation with air at 37°C and fully saturated with water, ii) 25 L min^{-1} nasal insufflation with air at approximately 20°C and 50% relative humidity, and iii) no nasal insufflation and breathing air at approximately 20°C and 50% relative humidity. They then cycled at three five-minute preset work-rates followed by a 15 min self-paced time-trial where they completed as much work as possible.

Results: When pre-treated with air at 37°C and fully saturated with water, there was a significant reduction of the respiratory exchange ratio throughout the pre-set work-rates ($P < 0.03$) and the amount of work completed in the time-trial was also significantly reduced ($P < 0.03$).

Conclusion: The possible mechanisms for these long term changes and their potential significance are discussed.

Key words: *nasal insufflation, oxygen uptake, respiratory exchange ratio, exercise performance*

Introduction

Nasal insufflation refers to the act of blowing air into the nose, specifically through non-sealed flexible cannulae. The flow of air typically exceeds peak inspiratory flow, which for adults is often >15 L min^{-1}. Recently, McGinley et al. [1] showed that insufflation of air at 20 L min^{-1} using non-sealed nasal cannulae dramatically relieved symptoms in patients with obstructive sleep apnoea or hypopnoea. Whilst there are many studies of the benefits of non-invasive respiratory support in cardiovascular and respiratory compromised individuals during the insufflation period [1, 2], little is known on what effects, if any, remain following the insufflation. Furthermore, the gas used by McGinley et al. [1] was warmed to 30 - 33 °C and at approximately 80% relative humidity (RH). The group presented a well-reasoned argument that the beneficial effects they observed in their patients were due to small increases in supra-pharyngeal pressure. Given this argument, one might question whether the additional effort of heating and humidification of an insufflation gas is required.

It is most appropriate to investigate the effects of insufflation on a clinically-compromised cohort. However, given the higher ethical cost attached to maximally stressing such a cohort and medical supervision needed this was not an option in the present study. The subjects used in the current investigation were all regularly undergoing similar maximal physical exertion as part of their sporting activities, and since the individuals all engaged in endurance events they were a homogenous group unlikely to be compromised by any residual cardio-respiratory limitations that may occur in the general population or respiratory patients. However, most interest in the effects of nasal insufflation is about how it influences the stressed cardio-respiratory axis of respiratory compromised individuals. In order to achieve cardio-respiratory stress in our athletic subjects they were instructed to undertake a fifteen minute self-paced time trial, exercise that uses these systems at near maximum aerobic capacity.

Therefore, the present study was carried out to investigate the effects of nasal insufflation of air at 25 L min^{-1}, 37°C and 100% RH on various cardio-respiratory variables in a group of male endurance athletes under respiratory stress. We extended the protocol of McGinley et al. [1] to include an additional test with

the same protocol as the main study except the insufflated gas was at ambient temperature and humidity.

Materials and methods

General Design

All exercise tests were carried out on an electrically-braked cycle ergometer (Lode Excalibur Sport, Netherlands). The protocol consisted of five visits. Visit 1 involved sub-maximal and maximal incremental cycling to determine maximal oxygen uptake ($\dot{V}O_2max$) and peak power output (PPO). Visits 2-5 involved cycling at three 5-minute progressive sub-maximal work-rates followed by a 15 minute time-trial where subjects completed as much work as possible. Prior to the exercise test one of three interventions was implemented: i) 30 minutes of nasal insufflation at 25 L min^{-1} with air at 37°C and fully saturated with water, ii) 30 minutes with nasal insufflation at 25 L min^{-1} of room air at approximately 20°C and 50% relative humidity, and iii) 30 minutes no insufflation and breathing room air at approximately 20°C and 50% relative humidity. Visit 2 served to familiarise the subject with the protocol and equipment, thereby minimising practice/learning effects and followed the same procedure as the control condition i.e. no insufflation followed by exercise. A randomised, cross-over design was used to eliminate any order effects, subjects completed the trials at the same time of day to eliminate any influence of circadian variation and trials were spaced 7 days apart.

Subjects

Eight healthy males ($\dot{V}O_2max$: 65 ± 8 ml·kg^{-1}·min^{-1}, PPO: 454 ± 60 W) competitive in cycling or triathlon volunteered their written informed consent to participate in the study. Their physical characteristics were age: 30 ± 6 yr, height: 179 ± 5 cm and body mass: 73 ± 5 kg. The study was performed according to the Declaration of Helsinki and was approved by the institution's Human Ethics Committee. All subjects were familiar with laboratory cycling and had completed a health questionnaire to rule out any obvious contra-indications for exercise.

Pre-Experimental Protocol

One week prior to the experimental trials, the sub-maximal test required each subject to cycle in a continuous, stepwise fashion for 6 minutes at four sub-maximal work-rates (100, 150, 200, and 250 W) at a constant, self-selected cadence. The $\dot{V}O_2max$ test followed, beginning 5 min after the last sub-maximal work-rate and required a linear increase in power from 100 W at 40 W·min^{-1} until volitional fatigue. A relationship between oxygen uptake in the last minute of each sub-maximal work-rate and power was developed and used to calculate a work-rate equivalent to 80% of $\dot{V}O_2max$ (289 ± 38 W). This is a standard protocol similar to those used previously e.g. [3].

Experimental Protocol

Subjects arrived at the laboratory after an overnight fast, having consumed 500 ml of water on the previous evening and on arising to ensure full hydration. To minimize differences and ensure adequate muscle glycogen concentrations, subjects avoided exercise for 24 h and food intake during the previous 24 h was recorded and subjects repeated this diet before subsequent tests; during this period, subjects also abstained from caffeine and alcohol. Subjects were instrumented whilst seated and baseline measures of heart rate, blood pressure and blood lactate were taken after they had remained stable for 5 minutes whilst resting. Subjects remained seated whilst one of the three interventions was performed, as described

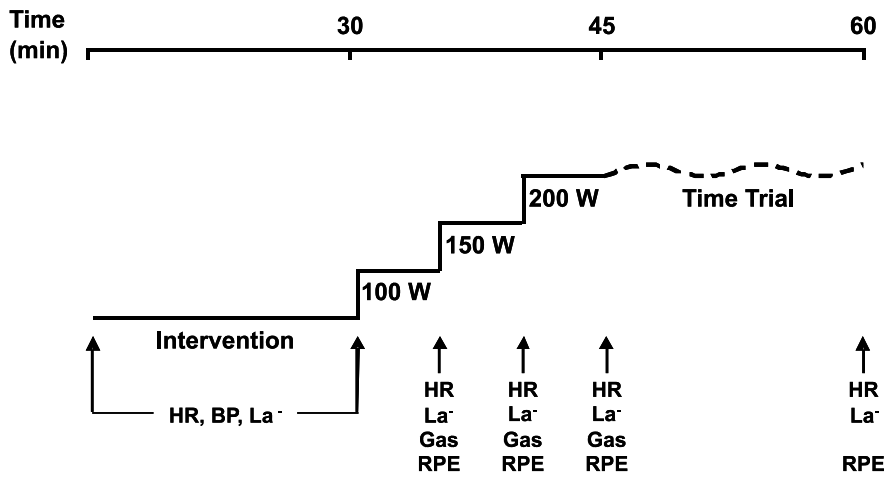

Figure 1. *Graphical representation of the experimental protocol. Abbreviations - HR: Heart rate, BP: Blood pressure, La-: Lactate, Gas: Expired gas, RPE: Rating of perceived exertion. Arrows indicate when measurements were made.*

above. When nasal insufflation was required this was generated using a PT100 humidifier blower system with a HC360 chamber and delivered to the subject using a 900PT500 heated breathing tube and a RT033 large nasal cannula. All humidification equipment was manufactured and provided by Fisher and Paykel Healthcare, New Zealand. In control experiments the subjects wore the apparatus but it was not turned on.

Subjects then cycled for three 5-minute progressive sub-maximal work-rates (100, 150 and 200 W), which were equal to 42 ± 10, 55 ± 11 and 67 ± 12 % $\dot{V}O_2$max. During these 15 minutes, the ergometer was set in hyperbolic mode so that the work rates were independent of cadence. At 15 minutes, the ergometer automatically changed to linear mode (work-rate was proportional to cadence in a relationship defined by the linear factor) and a 15-minute self-paced time trial (TT) was performed. The linear factor was calculated according to the formula:

$$W = L \cdot [rpm]^2$$

where *L* is the linear factor and was determined in a way where *W* represented the work rate eliciting 80% $\dot{V}O_2$max and *rpm* was the average pedalling rate during the final stages of the $\dot{V}O_2$max test. The TT required the subject to complete as much work as possible during the 15 minutes. Subjects were aware of every 5 minutes completed, however no verbal encouragement or other (physiological) feedback was provided.

During exercise testing, ambient temperature, relative humidity and air movement were held constant (20°C, 50% and 24 km h^{-1}, respectively).

Physiological Measures

A heart rate monitor (Polar Vantage NV, Finland) was placed around the chest for continuous monitoring. Blood pressure was assessed using a standard mercury gauge sphygmomanometer (Dekamet, Accoson, UK), with each reading repeated three times. Expired gas was collected using Douglas Bags and measured with an Ametek analyser (Applied Electrochemistry, USA) and a dry gas meter (Harvard, UK). Standard temperature pressure dry (STPD) values for VO_2, VCO_2 and respiratory exchange ratio (RER) were calculated. Glass capillary tubes were used to collect 50 µl of blood from the finger, with lactate concentration being determined by using a lactate auto-analyser (Yellow Springs Instruments, USA). Ratings of perceived exertion (RPE) were recorded using the CR-10 scale to assess the extent that central (cardiopulmonary [breathlessness]) and local (muscular [leg fatigue]) signals may contribute to global RPE [4].

Data and Statistical Analysis

A Shapiro-Wilk test was used to ensure data did not differ substantially from a Gaussian distribution. Analysis of variance (ANOVA) for repeated measures was carried out using SPSS (SPSS Inc., USA). Following a significant *F* test ($P < 0.05$), *post-hoc* comparisons were carried out using Student's paired *t*-tests with adjustment (Bonferroni correction) for multiple comparisons where appropriate ($P < 0.03$). When considering subject variability for the TT performance between conditions, individual (within-subject) coefficients of variation (CV) were calculated from the mean values (CV = [standard deviation/mean]·100). Values are reported as mean ± 1 standard deviation.

Results

Measures at Rest

The subjects reported no discomfort as a result of wearing the nasal prongs. Neither was the passage of air through the device, whether at ambient temperature or heated to 37°C and humidified to 100% RH perceived as unpleasant. The absence of (cardiovascular) stress was verified in that there were no changes in either heart rate (HR) or mean arterial blood pressure (MAP) following 30 minutes use of the device (control: 54 ± 6 beats min^{-1} and 92 ± 7 mmHg *vs.* humid air: 53 ± 6 beats min^{-1} and 92 ± 6 mmHg; $P > 0.05$).

Measures during Exercise

As expected, as work rate increased so did HR during exercise, such that expressed as a percentage of their maximum, subjects were working at 61 ± 6 % (100 W), 70 ± 6 % (150 W), 79 ± 6 % (200 W), 92 ± 5 % (289 ± 38 W) and 96 ± 3 % (end TT). However, nasal insufflation had no significant effect upon HR during exercise ($P > 0.05$).

Pulmonary ventilation increased with work rate (100 W: 41 ± 6 L min^{-1}, 150 W: 54 ± 11 L min^{-1}, 200 W: 72 ± 21 L min^{-1}) however nasal insufflation had no significant effect ($P > 0.05$). Blowing warmed, humidified air through the nares appeared to increase VO_2 and decrease VCO_2, although neither of these minor changes was statistically significant ($P > 0.05$). However, the RER was significantly altered when pre-treatment with warmed, humidified air was carried out ($P < 0.03$) with values for control of 0.904 ± 0.055 (100 W), 0.935 ± 0.050 (150 W) and 0.973 ± 0.067 (200 W) compared to 0.856 ± 0.053 (100 W), 0.904 ± 0.071 (150 W) and 0.932 ± 0.076 (200 W) with warm nasal humidification.

Whilst lactate concentrations were increased from resting values during exercise (rest: 1.4 ± 0.4 mmol L^{-1}, 100 W: 1.8 ± 0.9 mmol L^{-1}, 150 W: 2.0 ± 1.0 mmol L^{-1}, 200 W: 2.8 ± 1.7 mmol L^{-1} and end TT: 11.1 ± 1.7 mmol L^{-1}) warm nasal humidification had no effect ($P > 0.05$).

Subjects rated their perceived exertion, both for breathlessness and leg fatigue, as very weak (1.4 ±

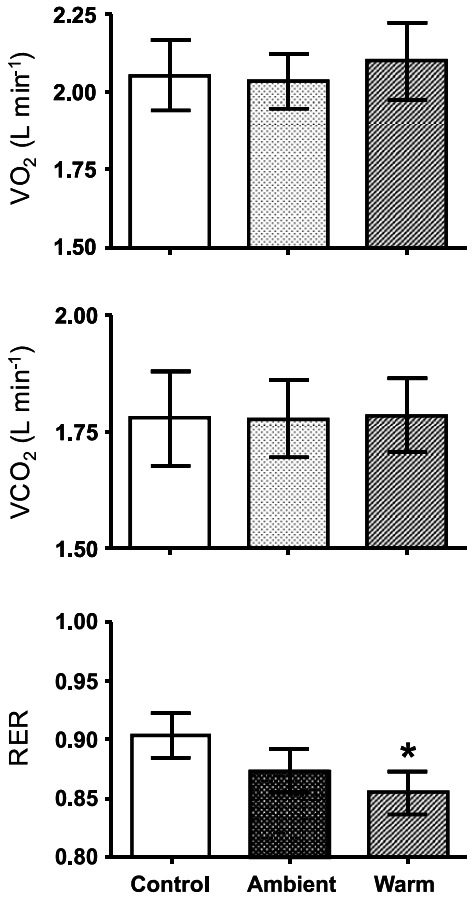

Figure 2. *The mean (± SD) O_2 uptake (VO_2), CO_2 production (VCO_2) and respiratory exchange ratio (RER) whilst exercising at 100 W. This is an example record; similar results were seen at all work-rates. *Significantly different to control condition ($P < 0.03$, $n = 8$).*

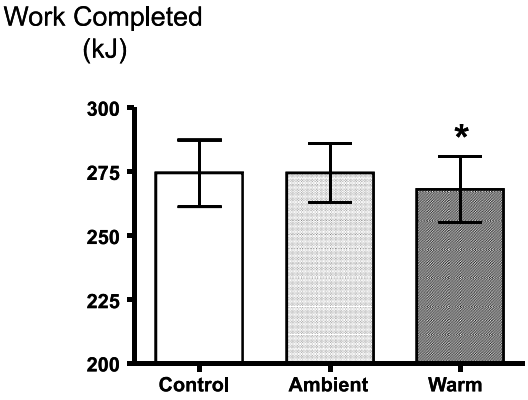

Figure 3. *The mean (± SD) total work achieved in a fifteen-minute time-trial. *Significantly different to control condition ($P < 0.03$, $n = 8$).*

0.8 units, 100 W), moderate (2.6 ± 1.3 units, 150 W), somewhat strong (3.9 ± 1.7 units, 200 W) and almost maximal (9.2 ± 1.2 units, end TT), however, nasal insufflation had no significant effect ($P > 0.05$).

The individual (within-subject) CV for the 15-minute TT was 1.7%. The total amount of work completed during the TT was significantly reduced following insufflation of warm humid air into the nose (control: 274 ± 37 kJ *vs.* warm nasal humidification: 268 ± 37 kJ; $P < 0.03$), a reduction of 2.2 ± 2.8%.

Discussion

Nasal instillation of air, whether at room temperature or warmed to body temperature and humidified, had no significant effect on any of the ventilatory or cardiovascular variables monitored. However, prior exposure to warm humidified air produced a significant reduction in the respiratory exchange ratio (RER) during working at preset exercise rates and a fall in the total work completed in a self-paced fifteen minute time-trial. Insufflation of air at room temperature had no significant effect. This indicates that the air needed to be warm to produce an effect. However, whether the protocol used by McGinley et al. [1] of 20 L min^{-1} at 30°C and 80% RH would have provoked these long term responses we observed or whether our more rigorous protocol of 25 L min^{-1} at 37°C and 100% RH was required was not tested. The mechanism by which the observed changes were produced was obscure. There appear to be two possibilities; either it was a direct mechanical effect of the insufflations or that they had provoked a long lasting reflex.

The benefits of high flow nasal insufflation and the mechanisms by which these occur are well known [5]. However, the mechanisms by which changes like reduction of nasopharyngeal dead space, inspiratory resistance and the energy cost of gas conditioning have only been investigated during the insufflation period [1, 2]. Whether a period of high flow nasal insufflation induces any long term physiological changes after the insufflation has ceased, investigated in the present study, does not appear to have been reported previously. It follows that we must use the acute studies as our starting point for comparative purposes. Nevertheless, such study comparisons must be made with some care as the projected outcomes are different.

The reduction in RER following insufflation of warm humid air was consistent. It could reflect a genuine reduction of the respiratory quotient (RQ), i.e. a change in the metabolic substrate being utilized but, equally well, either a reduction in CO_2 elimination or in increased oxygen uptake. Both were seen, although neither observation was significant. In a recent study it was shown that even modest nasal insufflations produced an increase in supraglottic (pharyngeal) pressure [1]. McGinley et al. [1] argue that, although these changes were small, they could have increased lung volume and, hence, oxygen stores and upper airway patency. They also suggest that there could have been a 'concomitant reduction in dead space ventilation'. All these factors would increase alveolar ventilation and, hence oxygen diffusion across the alveolar wall. This may, in part, explain the reduction in RER during the insufflation. The argument as to why such an improvement in lung function should be maintained after the insufflation was stopped is more tenuous.

Under most circumstances RER is regarded as an indicator of the RQ. RQ, when measured at a cellular or tissue level, reflects the substrate(s) that are being metabolised. The reduction of RER seen in the study may be seen to be indicative of a movement away from carbohydrate metabolism in favour of fatty acids being utilised as a metabolic substrate. However, there is a caveat to this proposal. If a previous exposure to nasal insufflation either increased oxygen uptake or reduced CO_2 elimination in the lung then there could, conceivably be a change in RER without there being any concomitant metabolic shift. A recent study has proposed the former could occur during the insufflation period [1].

It has been known for some time that stimulation of the nasal mucosa will provoke profound cardiovascular and respiratory reflexes [6[1], 7]. A number of studies have demonstrated nasal receptors responding to the flow of cold air through the nose which modify breathing. Cold air during the inspiratory phase of the breathing cycle has been shown to increase the sensation of nasal patency [8]. Whilst insufflations of warm humid air might be expected to reduce the stimulus to the nasal mucosa caused by breathing relatively cool and dry room air [9] no changes were observed in any of the ventilatory and cardiovascular variables measured in the present study. Whether there might be more subtle nasal reflexes that affect metabolism is not apparent from the literature.

The significant reduction in the total work completed in the self paced time trial was relatively small (2.2%). However, when considered over a one hour event, the increased time to the finish would be 79 seconds. This could result in the difference between winning and finishing well down the field; not an advantage for an athlete. Whether the reduced blood lactate seen in six of the eight subjects conferred any advantage is a point of conjecture. Whilst it has been shown that a reduced peak aerobic capacity is the most significant predictor of mortality in some respiratory diseases [10], the reduction in aerobic performance we observed in our athletes is unlikely to be of any consequence in the clinical setting. A maximum aerobic capacity < 60% of predicted norm is regarded as indicative of respiratory impairment in chronic obstructive pulmonary disease [11] and therefore aerobic performance changes ≈ 2% seen in the present study are probably of little consequence. Furthermore, the reduction in RER observed during the submaximal pre-set work-rates could be seen as advantageous to sedentary or clinical populations. A greater utilization of fat and sparing of carbohydrate stores could be seen as preferable for the continuation of an active lifestyle, and thus such nasal high flow therapy might be used as respiratory support during physical activity rehabilitation of patients with respiratory dysfunction.

Limitations and Considerations

The present study was carried out to extend the findings of McGinley et al. [1] to determine whether the effects they observed were maintained post-insufflation. It also included an additional test with the same protocol as the main study except the insufflated gas was at ambient temperature and humidity. Our study design could have included a further control condition where subjects received no insufflation but were breathing warmed, humidified air. This, however, would have substantially increased the time burden placed on our subjects who were receiving no compensation for participation, and whilst relevant for academic/scientific purposes would have limited ecological validity.

Conclusion

Insufflation of warm humidified air was well tolerated and the cardio-respiratory variables studied were not modified, either at rest or during exercise. However there was a significant maintained change in RER, possibly reflecting a change in metabolism. This effect, probably reflex in origin, persisted for some time after the exposure. Whether this phenomenon would also be seen in control (un-athletic) or a respiratory-compromised individual or for how long it is maintained is unknown and merits further study. Subsequent research in our laboratory will be directed to trying to establish the source of the effect by looking at nasal airway resistance and the temperature/humidity profile of the upper airways.

Acknowledgements

The authors would like to thank R. Hugh Morton for help provided with the study design, to those who helped with the data collection especially Matthew Barnes, and to the participants who gave their time and effort to undertake the study. Fisher and Paykel Healthcare Ltd, Auckland is gratefully acknowledged for provision of all humidification equipment.

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Received: December 28, 2009
Accepted: March 31, 2010-03-31
Published: April 09, 2010

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Conflicts of Interest

Other than the provision of humidification equipment by Fisher and Paykel Heathcare there are no conflicts of interest. At the time the experiments were completed Dr. Tatkov was an employee of Massey University.