Effects of Hyperoxia on Thermoregulatory Responses during Feet Immersion to Hot Water in Humans

Kazuaki Yamashita and Yutaka Tochihara

Department of Ergonomics, Kyushu Institute of Design

Abstract This study examined effects of hyperoxia on thermoregulatory responses. Eight healthy male students (23.5 ± 1.8 yrs) were involved in this study. They immersed their legs in a hot water bath (42°C) for 60 minutes in a climate chamber. The conditions of oxygen concentration of a chamber were set at 21% (control), 25% ($25\%\text{O}_2$), and 30% ($30\%\text{O}_2$). Ambient temperature and relative humidity was maintained at 25°C and 50% in every condition, respectively. Measurements included rectal temperature (T_{re}), skin temperature at 7 sites, laser Doppler flowmeter (LDF) on the back and forearm as an index of skin blood flow, heart rate, local sweat rate (Msw) on the back and forearm, and total body weight loss (BWL). Increases of T_{re} at $25\%\text{O}_2$ and $30\%\text{O}_2$ tended to be lower during the immersion than in the control. Mean skin temperature ($\bar{T}_{\text{sk}}$) of the control increased gradually after the onset of sweating, while the $\bar{T}_{\text{sk}}$ s at $25\%\text{O}_2$ and $30\%\text{O}_2$ maintained a constant level during sweating. LDFs on the forearm at $25\%\text{O}_2$ and $30\%\text{O}_2$ showed lower increases compared with the control. No significant differences in Msw on the back and the forearm and BWL were seen among the conditions. These results suggested that hyperoxia could not affect sweating responses but elicit an inhibitory effect on thermoregulatory skin blood flow. *J Physiol Anthropol Appl Human Sci* 22 (4): 181–185, 2003 <http://www.jstage.jst.go.jp/en/>

Keywords: hyperoxia, thermoregulation, heat exposure, skin blood flow, sweat rate

Introduction

Many reports have described the effects of hyperoxia on blood flow at various sites of the body. In previous studies, the effects of hyperoxia on blood flow in humans were observed as an increase in peripheral vascular resistance (Eggers et al. 1962; Crawford et al. 1997; Milone et al. 1999; Mak et al. 2002), reduction of blood flow on the forearm (Milone et al. 1999), brain (Nakajima et al. 1983), and thigh during exercise (Welch et al. 1977). This hyperoxic vasoconstriction (HV) has also been reported in isolated vessels (Carrier et al. 1964;

Messina et al. 1994; Pries et al. 1995; Mouren et al. 1997). Messina et al. (1994) demonstrated that diameter of isolated rat skeletal muscle arterioles decreased by 37% during the rise in oxygen tension of perfusate from 20 to 150 mmHg, with an additional decrease by 14% from 150 to 660 mmHg. These results indicate that hyperoxia could cause a reduction of systemic blood flow. Interestingly, Tomita et al. (1995) reported that vascular endothelial cells dilated and constricted during exposure to 0% and $100\%\text{O}_2$ stimulus, respectively. Moreover, they suggested that oxygen tension may contribute to capillary autoregulation of blood flow in the microvascular network.

Since the skin microvascular network consists of a rich microvascular bed, it was thought that hyperoxia could inhibit thermoregulatory blood flow in the skin. Additionally, the hyperoxic inhibition of skin blood flow may affect other thermoregulatory responses. There are, however, few reports on effects of hyperoxia on thermoregulatory responses. Therefore, the present study aimed at examining effects of hyperoxia on thermoregulatory responses in humans.

Methods

Subjects

Eight healthy male students (23.5 ± 1.8 yrs) were involved in this study. The purpose and procedure of the study were explained to each student before the experiments, and they consented to participate in the study voluntarily and were required to wear only shorts during the experiments.

Procedures

A climate chamber in which oxygen concentration (PO_2) in air could be controlled independently under normal air pressure was prepared for the experiments. The conditions of PO_2 were set at 21% (control), 25% ($25\%\text{O}_2$), and 30% ($30\%\text{O}_2$). Ambient temperature and relative humidity was controlled at 25°C and 50%, respectively. First, the subjects entered the climate chamber and sat for at least 20 minutes. After checking the stability of rectal and skin temperature, the subjects sat for 10 more minutes in order to measure resting states. Thereafter, for 60 min they immersed their legs in a hot

water bath maintained at 42°C. Each subject was exposed to three PO₂ conditions randomly and blindly on different days.

Measurements

Measurements included rectal temperature (Tre), skin temperature at 7 sites (forehead, chest, back, forearm, hand, thigh, and foot), laser Doppler flowmeter (LDF) on the back (LDFb) and forearm (LDFf), heart rate (HR), local sweat rates on the back (Mswb) and forearm (Mswf), and total body weight loss (BWL). For measurement of Tre, the subjects inserted a thermistor probe at the depth of 12 cm from the sphincter muscle. Thermistors were taped on the specified sites with surgical tape in order to measure skin temperature. Data regarding Tre and skin temperature were collected on a portable data logger (Gram, LT-8A) every second. Mean skin temperature ($\bar{T}_{sk}$) was calculated using the equation described by Shibasaki et al. (1997). Local sweat rate was measured using a ventilated capsule instrument (K&S, AMU-100II). LDF probes (omega flow, FLO-C1) were applied to adjacent sites to the ventilated capsules. Electrocardiogram (ECG) was obtained via a telemeter (DS-502, Fukuda Denshi). Each output voltage of each electrical device was recorded on a personal computer (PC-286VF, EPSON) at 500 Hz via an A/D converter (microscience, ADM-5298BPC). In off-line works, R-R intervals were obtained from the ECG, and HR was calculated based on R-R intervals. BWL was determined as the gap between the body weight before and after the experiments, obtained by means of a sensitive balance (ID2, Mettler Instrumente) with an accuracy of ± 1 g.

Statistics

All statistical analyses were performed using STATISTICA for Windows ver. 5.1J (StatSoft, Inc.). Data from time-course measurements were evaluated using repeated measures two-way analysis of variance (ANOVA) employing the data taken every 2 minutes. The effect of PO₂ on BWL was assessed by means of one-way ANOVA. Post-hoc test was performed using Fisher's protected least significant difference for multiple comparisons. Significant differences were established at the $p < 0.05$ level. Each figure is shown as mean values and standard deviation.

Results

Figure 1 illustrates time course of Tre. Two-way ANOVA revealed a significant main effect of time ($F(34, 238) = 98.51$, $p < 0.001$) and interaction between conditions and time ($F(68, 476) = 2.28$, $p < 0.001$) on Tre. Although Tre rose due to immersion in every condition, the increase in Tre at 25%O₂ and 30%O₂ was smaller than that of the control. The time course of $\bar{T}_{sk}$ is shown in Figure 2. Two-way ANOVA revealed a significant main effect of time ($F(34, 238) = 12.12$, $p < 0.001$) and interaction between conditions and time ($F(68, 476) = 1.48$, $p < 0.05$) on $\bar{T}_{sk}$. $\bar{T}_{sk}$ s of 25%O₂ and 30%O₂ decreased from the onset of sweating and then maintained a constant level

Fig. 1 Time course of rectal temperature of control, 25%O₂ and 30%O₂. Values are means $\pm$ SD. "time: $p < 0.01$ " indicates a significant main effect of time. "cond * time: $p < 0.01$ " indicates a significant interaction between conditions and time.

Fig. 2 Time course of mean skin temperature of control, 25%O₂ and 30%O₂. Values are means $\pm$ SD. "time: $p < 0.01$ " indicates a significant main effect of time. "cond * time: $p < 0.05$ " indicates a significant interaction between conditions and time.

during the immersion, while the $\bar{T}_{sk}$ of the control increased gradually after the onset of sweating. Figure 3 illustrates the time course of LDFb, LDFf, Mswb, and Mswf. As the results of two-way ANOVA, a significant interaction between conditions and time was observed on LDFf ($F(68, 476) = 1.54$, $p < 0.01$), while no significant interaction was seen between conditions and time on LDFb, Mswb, and Mswf. LDFfs of 25%O₂ and 30%O₂ tend to increase to a lesser degree than that of the control. The immersion elicited an increase of HR of 18.3 ± 7.3 bpm, 15.4 ± 8.0 bpm, and 17.6 ± 4.8 bpm in the control, and at 25%O₂, and 30%O₂, respectively, but a noticeable difference was not observed in HR. BWL of each condition was 270.3 ± 65.8 g in the control, 252.4 ± 56.2 g in 25%O₂ and 259.0 ± 59.5 g in 30%O₂, while no significant differences were seen regarding BWL.

Fig. 3 Time course of LDF and local sweat rate on the back and forearm of control, 25%O₂ and 30%O₂. Values are means±SD. "time: $p<0.01$ " indicates a significant main effect of time. "cond * time: $p<0.01$ " indicates a significant interaction between conditions and time.

Discussion

Several reports have described the effects of hyperoxia on sweat rate. Hubbard and Weiner (1969) showed that there were no significant differences in the forearm sweat rate between breathing 10.5% and 100%O₂ under 2ATA. Dikshit et al. (1980) demonstrated that there were no significant changes in the whole body sweat rate during 100%O₂ breathing compared with ordinary air breathing under an extremely hot environment of 57°C. On the other hand, Iyer et al. (1983) showed a significant increase in the forearm sweat rate by breathing 100%O₂ under the same thermal condition as reported by Dikshit et al. (1980), although no significant differences were observed regarding whole body sweat rate. The present study's results regarding forearm sweat rate are consistent with the results reported by Hubbard and Weiner (1969), but not those of Iyer et al. (1983). This discrepancy may depend on the difference of thermal condition, i.e., the thermal stress involved in the study by Iyer et al. (1983) was considerably higher compared with that of the present study. In fact, whole body sweat rate reported by Iyer et al. (1983) was 531 ± 145 g and 543 ± 143 g in normal air and 100%O₂ breathing, respectively, which is about twice that of the BWL observed in the present study.

A major point of interest in the present study regards the effects of hyperoxia on thermoregulatory skin blood flow. Many researchers have assessed HV at various sites of the

body during rest. Milone et al. (1999) reported a significant decrease of forearm blood flow during breathing 100%O₂ in comparison to breathing normal air. Some researchers have also shown similar hyperoxic effects on forearm blood flow (Eggers et al. 1962; Mak et al. 2002). Additionally, reports have described the reduction of blood flow during hyperoxia in the calf (Reich et al., 1970; Hansen and Madsen, 1973), in the retina (Dallinger et al. 2000), the brain (Nakajima et al. 1983), and the subcutaneous adipose tissue (Hansen et al. 1976). The mechanisms of HV have been discussed from various standpoints. One potential mechanism may be a dysfunction of endothelium-derived relaxing factors (EDRF) by reactive oxide species (Rubanyi and Vanhoutte 1986). On the other hand, recent studies revealed that nitric oxide (NO), which is an EDRF, played a critical role in thermoregulatory skin vasodilatation (Dietz et al. 1994; Shastry et al. 1998; Kellogg Jr. et al. 1998; Schmid et al. 1998; Shastry et al. 2000). If HV brings about a dysfunction regarding NO, it is conceivable that thermoregulatory skin blood flow also suffers from hyperoxia. However, Mouren et al. (1997) suggested that HV was not eliminated by inhibition of NO synthesis in vitro. Hence, it is unlikely that HV is caused by NO dysfunction alone.

In the present study, $\bar{T}_{\text{sk}}$ s at 25%O₂ and 30%O₂ maintained lower levels than did the control as shown in Figure 2, and increase in LDFf was smaller at 25%O₂ and 30%O₂ compared with the control (Fig. 3). Since there were no significant differences between local sweat rate and BWL, it was

estimated that evaporative heat loss was approximately equal in each condition. Therefore, lower $\bar{T}_{\text{sk}}$ at 25%O₂ and 30%O₂ may be induced by a lower increase of skin blood flow. As shown in Figure 1, increases of T_{res} at 25%O₂ and 30%O₂ tend to be smaller than in the control. These results may also be interpreted to be elicited by HV, i.e., lower skin blood flows on the lower limbs in 25%O₂ and 30%O₂ may intercept the heat gain from hot water to the limbs.

Previous studies have frequently utilized the method of breathing 100%O₂ to create a hyperoxic condition (e.g., Milone et al. 1999). As an interesting observation of this study is that even 25% or 30%O₂ breathing could induce HV in skin blood flow. On the other hand, there were no significant differences in thermoregulatory responses between 25%O₂ and 30%O₂. It is unclear that a gap of 5%O₂ concentration is sufficient to elicit differences in thermoregulation during hyperoxia, or whether the thermoregulatory effects of hyperoxia were saturated in 25%O₂. In order to answer these questions, further study is needed involving higher O₂ concentrations.

In summary, lower $\bar{T}_{\text{sk}}$ and LDF_f were observed at 25%O₂ and 30%O₂ compared with the control. Since there were no significant differences in M_{swb} , M_{swf} , and BWL among the conditions, it was estimated that evaporative heat loss in each condition was approximately equal. Therefore, lower $\bar{T}_{\text{sk}}$ during hyperoxic conditions may indicate that thermoregulatory skin vasodilatation was inhibited by hyperoxia. In conclusion, it was suggested that the inhibitory effects of hyperoxia on blood flow could not affect sweating responses but thermoregulatory skin blood flow in hyperoxic conditions.

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Correspondence to: Kazuaki Yamashita, 4–9–1 Shiobaru, Minami-ku, Fukuoka 815–8540, Japan
Phone: +81–92–553–4522
Fax: +81–92–553–4569
e-mail yam@rms.kyushu-id.ac.jp