SAFETY AND EXERCISE PRESCRIPTION FOR HIGH-ALTITUDE MOUNTAINEERING IN TRANSPLANT PATIENTS: THE "MONTE ROSA" PROJECT

Dorelli G.[1,2], Savoldelli A.[2,3], Fornasiero A. [2,3], Callovini A. [2,3], Decet M.[2], Pellegrini B. [2,3], Vanoni L.[4], Schena F.[2,3], Dalle Carbonare L.[1],

[1]Department of Medicine, School of Medicine in Sports and Exercise, University of Verona, Italy. [2]CeRiSM, Sport Mountain & Health Research Centre, University of Verona, Rovereto, Italy. [3]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Italy. [4]National Medical Commission of the Italian Alpine Club, Milan, Italy

Introduction

In recent years the quality of life in patients after transplantation has improved, allowing these patients to do physical activity without significant limitations. However, due to the physiological alterations and the potential systemic comorbidities of transplant patients, the safety and feasibility of high-intensity exercise in an extreme environment such as high altitude mountaineering present some critical issues.

Patients with cystic fibrosis (CF), heart disease, and ineffective ventilation have a reduced capacity to tolerate altitude changes, especially during demanding exertion.[1]

Acute mountain sickness (AMS), no matter the fitness and the health status, is a potential limiting condition in addition to the technical difficulties and the physical commitment that high-altitude trekking requires.[2]

Therefore, in solid organ transplant patients who want to approach high-altitude mountaineering, we think it is necessary to evaluate three aspects:

1. the cardio-respiratory condition that may be hazardous, or a limit, during high-intensity physical activity and that could be worsened by hypoxia
2. the fitness level and the ventilatory thresholds (VT1 and VT2): for both training and effort management.
3. the susceptibility to acute mountain sickness, especially for trekking at altitudes above 2500 meters

Our study wants to evaluate these aspects in a small population of transplanted patients and correlate the data with the physiologic adaptations of these subjects during an alpine expedition up to 4500 meters.

Methodology

A group of four transplant recipients and one patient with cystic fibrosis without lung transplantation (total: 5 subjects; 2 males, 3 females) went under a medical examination and an incremental cardiopulmonary exercise test (CPET) with step protocol during walking on an inclined (25%) treadmill both in normoxia (N) and in normobaric hypoxia (H; FiO2 range: 12.1%-12.9%, 3827 - 4333 m). Electrocardiography (ECG) and arterial oxygen saturation (SaO_2) were registered during exercise tests.

Susceptibility to acute mountain sickness (AMS) was determined with the mean of SaO_2 values 20 and 30 minutes after exposure to the simulated normobaric hypoxia, according to Butscher et al. [2]

Each patient performed the visit and all tests on the same day. The tests were carried out in mid-June 2021. After one month the patients attempted a two-days high-altitude expedition to the Capanna Regina Margherita hut (4554 meters above sea level, a.s.l.), spending the night at Capanna Gnifetti Hut (3647 meters a.s.l.). During the expedition, we gave medical assistance and monitored SaO_2 at different altitudes. The symptoms of AMS were reported according to the 2018 Lake Louise Acute Mountain Sickness Score.[3] We monitored SaO_2 and AMS also in 5 healthy control subjects.

Results

One patient underwent kidney transplantation due to membranoproliferative glomerulonephritis. One had lung transplantation for idiopathic pulmonary hypertension, and three patients had CF with diabetes and took insulin. Two out of three CF patients had lung transplantation. Four patients (80%) had arterial hypertension, one (20%) was using beta-blockers and four (80%) were pharmacologically immunosuppressed. No one had a clinical and a family history positive for cardiomyopathy.

Maximal oxygen consumption (VO_2max; N: 42.2 ± 10.8; H: 29 ± 6.2 mLO2/min/kg), maximal heart rate (N: 162 ± 24; H: 149 ± 26 bpm) and minimal SaO_2 (N: 92 ± 7; H: 81±4 %) were lower ($p<0.05$) in the simulated altitude. There were no statistical differences between the resting ECG measures.

Three out of five (60%) subjects showed isolated, monomorphic premature ventricular beats (PVB) with common morphology during the exercise and one subject showed coupled PVBs only during the hypoxic condition. In this patient, cardiac imaging and blood routine tests excluded cardiac and hormonal alterations.

Table 1. Cardiopulmonary and ECG data

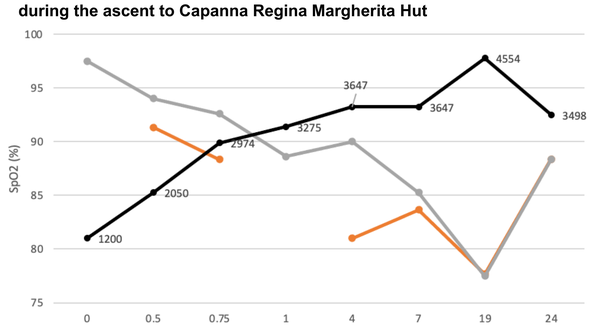
	Normoxia	Hypoxia	p-value
VO2max, mL/min/Kg	42.2 ± 10.8	29 ± 6.2	<0.05
Maximal heat rate	162 ± 24	149 ± 26	<0.05
SpO2 at peak, %	92 ± 7	81±4	<0.05
VT1 relative to VO2max, %	68 ± 7	78 ± 13	<0.05
VT2 relative to VO2max, %	86 ± 3	84 ± 13	0.43
PR interval, s	0,16 ± 0,02	0,16 ± 0,02	0,79
QRS duration, s	0,069 ± 0,007	0,073 ± 0,007	0,09
QTc interval	0,40 s ± 0,03	0,42 s ± 0,04	0,28
premature ventricular beats (PVBs), n	9	14	
complexity of PVB	no	yes	

Two subjects were susceptible to AMS during the simulated exposure (Table 2), but only one of them experienced mild AMS above 4000 m (Lake Louise AMS Score: 4). Two subjects out of five reached the summit (the cystic fibrosis patient without lung transplantation and the kidney recipient) with a mean SaO2 of 77.5, similar to that measured in control subjects (see Figure 1). One transplant patient stopped at 3700 m due to abdominal pain, while two withdrew at 4000 m due to low-temperature problems. VO_2max (N) was higher in the patients that completed the ascent (48.9 ± 8.7 versus 37.8 ± 1.4 mLO_2/min/kg).

Table 2. Susceptibily to AMS, according to Burtscher (2004)

	SpO_2 20' (%)	SpO_2 30'(%)	mean SpO_2 (%)	simulated altitude (m)	AMS
CS	**78**	**79**	**79**	**3827**	**+**
TA	89	90	90	3950	-
LV	82	87	85	3888	±
ZG	**80**	**80**	**80**	**4204**	**+**
DM	83	83	83	4139	±

Figure 1. Mean SaO_2 in transplant patients ( ) and the control group ( ) during the ascent to Capanna Regina Margherita Hut



Conclusion

Based on our experience, we can state that transplant recipients and CF patients can perform high altitude mountaineering with the proper training and evaluation. According to available data, our findings suggest that hypoxia may lower intracellular O2 availability, altering myocardium excitatory properties (we found an increase in the number of PVBs and their complexity)[4].

In our study, the success rate of the expedition was determined mainly by the fitness level of the subjects and the susceptibility to AMS played a minor role: SaO2 decreases equally in both patients and healthy controls.

Our study has many limitations and the small sample size does not allow us to obtain definitive conclusions. However, according to the available evidence, we suggest that transplant patients can deal with high altitude mountaineering and simulated hypoxia testing could be decisive in clinical and training decisions.

References

1. Weber, U. *et al.* High altitude trekking after lung transplantation: a prospective study using lung ultrasound to detect comets tails for interstitial pulmonary edema in lung transplant recipients and healthy volunteers. *Transpl. Int.* **31**, 1245–1253 (2018).
2. Burtscher, M., Flatz, M. & Faulhaber, M. Prediction of susceptibility to acute mountain sickness by SaO2 values during short-term exposure to hypoxia. *High Alt. Med. Biol.* **5**, 335–340 (2004).
3. Roach, R. C. *et al.* The 2018 lake louise acute mountain sickness score. *High Alt. Med. Biol.* **19**, 4–6 (2018).
4. Coustet, B., Lhuissier, F. J., Vincent, R. & Richalet, J. P. Electrocardiographic changes during exercise in acute hypoxia and susceptibility to severe high-altitude illnesses. *Circulation* **131**, 786–794 (2015).