



Review

Using a new plateau hyperbaric chamber to alleviate high altitude hypoxia: Rabbit and human studies



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ABSTRACT

Objectives: To validate the effects of the new plateau hyperbaric chamber on alleviating high altitude hypoxia on Mount Kun Lun.

Methods: A prospective, controlled study of rabbits and adult volunteers was conducted at altitudes of 355, 2880 and 4532 m. We obtained arterial blood samples from rabbits and volunteers before and after hyperbaric treatment. The respiratory rate, heart rate, and blood pressure (BP) of adult volunteers were monitored during hyperbaric treatment. **Results:** The mean PaO₂ levels of experimental group rabbits and volunteers increased significantly after 60 min of hyperbaric treatment at 350, 2880 and 4532 m. The mean PaCO₂ and pH levels of rabbits were not significant different before and after hyperbaric treatment at each altitude. The mean PaCO₂ and pH levels were not significant different at 355 m in the human study. However, at 2880 and 4532 m, pH fell with increasing PaCO₂ levels in humans before and after hyperbaric treatment.

Conclusions: The new multiplace plateau hyperbaric chamber may be used to alleviate plateau hypoxia by increasing patient PaO₂. However, its value in treating AMS must be confirmed in field conditions.

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Contents

1. Introduction	1537
2. Ethics statement	1537
3. Methods	1537
3.1. Study design	1537
3.1.1. Animal experiments	1537
3.1.2. Human experiments	1538
3.2. Statistical analyses	1538
4. Results	1538
4.1. Results of animal experiments	1538
4.2. Results of human experiments	1538
4.3. Adverse events	1539
5. Discussion	1539
5.1. Limitations	1541
5.2. Conclusions	1541
Acknowledgements	1541
References	1541

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1. Introduction

Although the pathophysiology of acute mountain sickness (AMS) has not been completely clarified, hypobaric hypoxia is thought to play a predominant role [1]. The partial pressure of atmospheric oxygen falls progressively as barometric pressure decreases with increasing altitude. Therefore, descent is lifesaving when severe symptoms suggest the onset of AMS. If descent is not possible, simulated descent through pressurization in a hyperbaric chamber is equally effective in the treatment of AMS.

The Gammow bag is the most important and popular device used in most trekking and high altitude expeditions to treat and prevent AMS [2–4]. The Gammow bag is an inflatable cylindrical tube made of heavy rubber or durable fabric that pressurizes the atmosphere sealed within it to that of a much lower altitude.

However, treatment of sick subjects within the very confined space of the chamber can be difficult, and prolonged treatment makes considerable demands on the individuals required to maintain pressure with the foot pump [5]. Particularly, the Gammow bag is not always an acceptable therapy alternative in a predominantly elderly population. Moreover, most types of portable hyperbaric chambers are monoplace chambers. If many patients suffer from AMS, such as laborers and soldiers, the portable hyperbaric chamber may be ineffective.

The efficacy of hyperbaric oxygen therapy has been validated by extensive clinical experience and scientific studies for decompression sickness and high-altitude illnesses [6–7]. However, the potential risks, shortage of oxygen supply, and complexity of using hyperbaric oxygen have limited its application in the treatment of AMS.

Like other portable hyperbaric chambers, based on the principle of increasing ambient pressure within the chamber, a new multiplace plateau hyperbaric chamber has been designed to satisfy the needed of patients who suffer from AMS (Fig. 1). Unlike other portable hyperbaric chamber, atmospheric pressure is increased by adjusting the opening of the expiration valve in proportion to the ambient pressure. Hence, carbon dioxide (CO_2) inside the chamber will not be accumulated during pressurization. We have demonstrated the safety and convenience of the chamber and have suggested possible applications for the chamber in AMS treatment [8]. During pressurization, the minimum pressure of the main compartment can reach up to 0.029 MPa at 355 m, 0.022 MPa at 2880 m and 0.02 MPa at 4532 m. In the current study, further research on rabbits and adult volunteers will be conducted to validate the effects of the chamber on alleviating high altitude hypoxia on Mount Kun Lun.



Fig. 1. The new multiplace plateau hyperbaric chamber (1 = Compressor; 2 = Doors; 3 = Control device; 4 = Desk; 5 = Beds; 6 = Gas vent; 7 = Air evacuation valve; 8 = Windows; 9 = Main compartment; 10 = Buffer compartment; 11 = Intake-tube; 12 = Silencer). Minimum pressure of the main compartment can reach up to 0.029 MPa at 355 m, 0.022 MPa at 2880 m and 0.02 MPa at 4532 m.

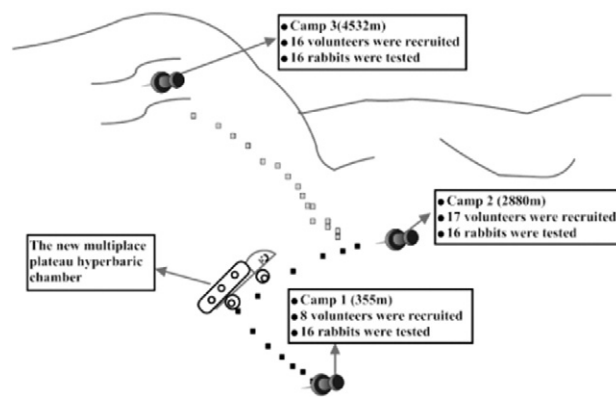


Fig. 2. The location, altitude, and volunteer recruitment at various altitudes between Xi'an City and the Kun Lun Mountains.

2. Ethics statement

Animal and human experiments inside the plateau hyperbaric chamber were performed at altitudes of 355, 2880 and 4532 m (Fig. 2). Experiments were approved by the Ethical Review Board of the General Hospital of Chinese People's Armed Police Force. In animal experiments, operative procedures and animal care were performed in compliance with national and international regulations (Italian Regulation D.L.vo 116/1992 and European Union Regulation 86/609/EC). The protocol was examined and approved before the start of the study by the Ethics Committees, Animal Facility of General Hospital of Chinese People's Armed Police Force. The recommendations of the ARRIVE guidelines in animal research were also consulted and considered [9].

In human experiments, volunteers were given written information and a verbal explanation concerning the study before obtaining written informed consent for their participation. Before commencement of the study, all volunteers were fully informed and signed an informed consent document.

3. Methods

3.1. Study design

3.1.1. Animal experiments

Sixteen adult male rabbits were used for the experiment at each altitude. The animals were purchased from a laboratory animal supplier (Animal experiment center of Xi'an Jiaotong University Health Science Center and Ma Wang Zhen rabbit farm of Xi'an City). All animals were anesthetized using 2% pentobarbital sodium (Sigma, USA). Under general anesthesia, a tracheotomy was performed 1-cm dorsal from the cricoid and a tracheal tube with 3.5-mm internal diameter and 14-cm length portex tracheal tubes (SIMS Portex, Portex) was inserted into the trachea. Then, an arterial indwelling catheter was inserted into the right carotid artery. After the operation, the first arterial blood samples were collected from the rabbit carotid arterial indwelling catheters. Then, eight rabbits of the experimental group were placed into the plateau hyperbaric chamber and underwent hyperbaric treatment. Eight rabbits of the control group breathed ambient air. The second arterial blood samples of the experimental group were collected after 60 min of hyperbaric treatment. The second arterial blood samples of the control group were collected after 60 min of exposure to ambient air. These samples were measured immediately, in all cases, the time elapsed between sampling and analysis was <1 h.

Arterial blood samples were analyzed with the use of a portable blood gas analyzer (i-STAT 200, Abbott Point of Care Inc., USA). The PaO_2 , PaCO_2 , and pH levels were measured. The blood gas analyzer was altered from its original specification so that it would function at high altitude. This modification was necessary to circumvent an inbuilt

mechanism that prevented the analysis of samples at barometric pressures lower than 400 mmHg (53.3 kPa).

3.1.2. Human experiments

Volunteers were recruited at 355, 2880 and 4532 m for the present study. All participants were medically evaluated to exclude those with acute or chronic conditions that could increase the risk of harm from exposure to the hyperbaric chamber. The selection criteria included the following: 1) ethnic Han; 2) residence in the highlands for at least four weeks preceding the study; and 3) arrival from a low-altitude province (<2500 m). Potential participants were excluded if they had AMS, signs and symptoms of a substantial acute infection, additional physical training or were scheduled to gain or lose weight, or any known cardiac, pulmonary, or other chronic diseases that would render them at increased risk of altitude illness.

Each participant took part in only one test session. After being informed, testers and participants entered the chamber and closed all doors. At the beginning of each session, participants were instructed to breathe regularly and quietly in a sitting position. After 60 min of rest, the first arterial blood samples were collected from the radial artery. Then, the chamber was pressurized with an electrically driven centrifugal compressor. Participants spent most of the time in assigned seats but were encouraged to walk or stand when involved in a test activity. Respiratory rate (RR), heart rate (HR) and blood pressure (BP) of the participants were monitored during hyperbaric treatment. RR, HR and BP were recorded before and after 60 min of hyperbaric treatment. The second arterial blood samples were collected from each participant after 60 min of hyperbaric treatment. The blood samples were analyzed immediately in the hyperbaric chamber, in all cases, the time lapse between sampling and analysis was under 1 h.

Arterial blood samples were analyzed using a portable blood gas analyzer (i-STAT 200, Abbott Point of Care Inc., USA). PaO_2 , PaCO_2 , and pH levels were measured. RR and HR were monitored by fingertip pulse oximetry (Pulsox-3i, Minolta, Osaka, Japan). Blood pressure (BP) was measured by the Riva-Rocci Sphygmomanometer.

3.2. Statistical analyses

The SPSS statistical software package 20.0 and GraphPad Prism V4.0 were used to perform the statistical analyses. Data are presented in a descriptive fashion (mean \pm standard deviation [SD] or median with range). The significance of differences between the two groups was tested using the independent two-sample *t*-test or the Mann–Whitney *U*

test. Qualitative and non-normally distributed data were analyzed with nonparametric statistics. A statistically significant difference was defined by $p < 0.05$.

4. Results

4.1. Results of animal experiments

Forty-eight healthy male rabbits were used. Sixteen were used at 355 m (2.15 ± 0.53 kg, ranging from 2.0 to 2.5 kg), 16 were used at 2880 m (2.02 ± 0.34 kg, ranging from 2.0 to 2.5 kg), and 16 were used at 4542 m (2.03 ± 0.65 kg, ranging from 1.9 to 2.3 kg).

The arterial blood gas analysis results (PaO_2 , PaCO_2 and pH levels) of the experimental group at different altitudes are shown in Fig. 3. After 60 min of hyperbaric treatment, the mean PaO_2 level rose from 68.63 ± 3.89 to 115.38 ± 5.76 mmHg at 355 m, from 43.38 ± 8.07 to 80.63 ± 7.99 mmHg at 2880 m, and from 34.75 ± 3.88 to 72.88 ± 8.76 mmHg at 4532 m. There were no significant differences in mean PaCO_2 and pH levels before and after hyperbaric treatment.

The arterial blood gas analysis results (PaO_2 , PaCO_2 and pH levels) of the control group at different high altitudes are shown in Fig. 4. After 60 min of exposure to room air, the mean PaO_2 level rose from 65.86 ± 7.30 to 80.75 ± 7.44 mmHg at 355 m, from 39.25 ± 4.68 to 55.00 ± 8.21 mmHg at 2880 m, and from 32.25 ± 2.49 to 48.50 ± 4.00 mmHg at 4532 m. There were no significant differences in mean PaCO_2 and pH levels before and after exposure to room air.

The mean PaO_2 levels of experimental and control group rabbits after 60 min of intervention (hyperbaric treatment or exposure to room air) at different altitudes are shown in Fig. 5. The mean PaO_2 levels were higher in the experimental group than in the control group at each altitude.

Changes in PaO_2 with increasing pressure inside the chamber at different altitudes are shown in Fig. 7 (A). PaO_2 was progressively limited with increasing altitude, decreasing linearly by a factor proportional to the pressure inside the chamber.

4.2. Results of human experiments

Volunteers in this study were 33 healthy men. Eight men were recruited (age 29.2 ± 3.46 , between 26 and 35 years of age) at 355 m, 17 men were recruited (age 19.2 ± 1.93 , between 18 and 22 years of age) at 2880 m, and 16 men were recruited (between 18 and 22 years of age) at 4542 m.

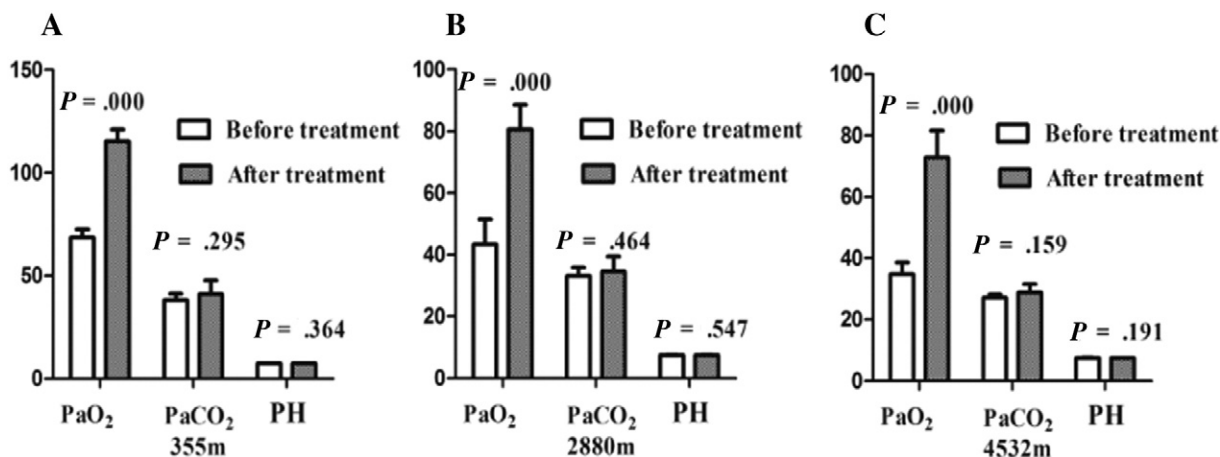


Fig. 3. PaO_2 , PaCO_2 and pH levels of experimental group rabbits at different high altitudes: (A) At 355 m, after 60 min of hyperbaric treatment, the mean PaO_2 level rose from 68.63 ± 3.89 to 115.38 ± 5.76 mmHg ($t = -19.036$, $P = 0.000$), the mean PaCO_2 level rose from 38.09 ± 3.09 to 40.94 ± 6.74 mmHg ($t = -1.087$, $P = 0.295$), and the mean pH fell from 7.43 ± 0.05 to 7.40 ± 0.06 ($t = 0.938$, $P = 0.364$). (B) At 2880 m, after 60 min of hyperbaric treatment, the mean PaO_2 level rose from 43.38 ± 8.07 to 80.63 ± 7.99 mmHg ($t = -9.272$, $P = 0.000$), the mean PaCO_2 level rose from 33.00 ± 2.83 to 34.50 ± 4.87 mmHg ($t = -0.753$, $P = 0.464$), and the mean pH fell from 7.49 ± 0.06 to 7.47 ± 0.07 ($t = 0.617$, $P = 0.547$). (C) At 4532 m, after 60 min of hyperbaric treatment, the mean PaO_2 level rose from 34.75 ± 3.88 to 72.88 ± 8.76 mmHg ($t = -11.257$, $P = 0.000$), the mean PaCO_2 level rose from 27.13 ± 0.99 to 28.75 ± 2.82 mmHg ($t = -1.540$, $P = 0.159$), and the mean pH fell from 7.52 ± 0.08 to 7.47 ± 0.04 ($t = 1.374$, $P = 0.191$).

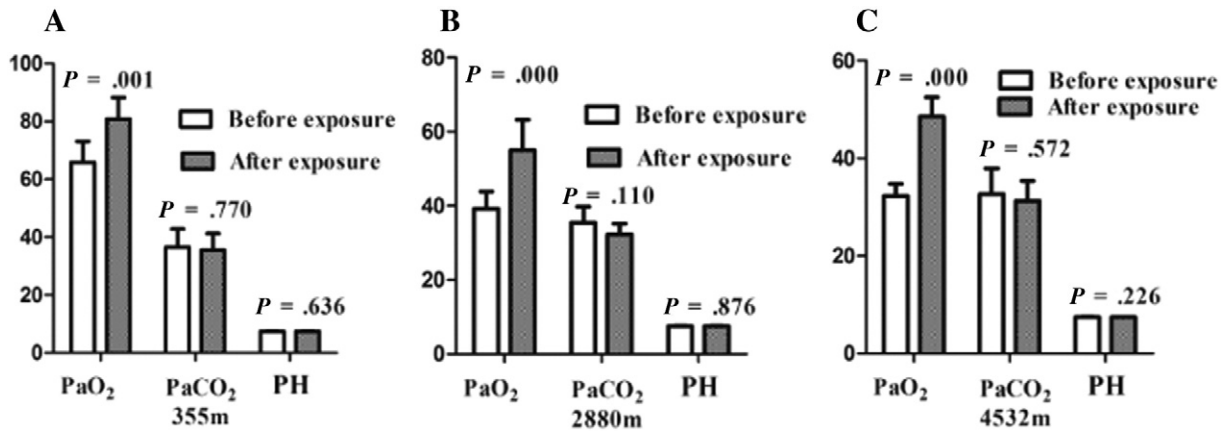


Fig. 4. PaO₂, PaCO₂ and pH levels of control group rabbits at different high altitudes: (A) At 355 m, after 60 min of exposure to room air, the mean PaO₂ level rose from 65.86 ± 7.30 to 80.75 ± 7.44 mmHg ($t = -4.042$, $P = 0.001$), the mean PaCO₂ level fell from 36.46 ± 6.36 to 35.56 ± 5.67 mmHg ($t = 0.299$, $P = 0.770$), and the mean pH rose from 7.45 ± 0.06 to 7.46 ± 0.06 ($t = -0.483$, $P = 0.636$). (B) At 2880 m, after 60 min of exposure to room air, the mean PaO₂ level rose from 39.25 ± 4.68 to 55.00 ± 8.21 mmHg ($t = -4.713$, $P = 0.000$), the mean PaCO₂ level fell from 35.50 ± 4.28 to 32.25 ± 3.28 mmHg ($t = -1.705$, $P = 0.110$), and the mean pH rose from 7.49 ± 0.05 to 7.50 ± 0.04 ($t = -0.159$, $P = 0.876$). (C) At 4532 m, after 60 min of exposure to room air, the mean PaO₂ level rose from 32.25 ± 2.49 to 48.50 ± 4.00 mmHg ($t = -9.752$, $P = 0.000$), the mean PaCO₂ level fell from 32.63 ± 5.29 to 31.25 ± 4.13 mmHg ($t = 0.612$, $P = 0.572$), and the mean pH rose from 7.47 ± 0.06 to 7.44 ± 0.03 ($t = 1.267$, $P = 0.226$).

The results of the arterial blood gas analyses (PaO₂, PaCO₂ and pH) of the volunteers at different altitudes are shown in Fig. 6. After 60 min of hyperbaric treatment, the mean PaO₂ level rose from 96.38 ± 9.80 to 148.38 ± 16.94 mmHg at 355 m, while mean PaCO₂ and pH levels were not significantly different. However, at 2880 m and 4532 m, when the mean PaO₂ level rose significantly, the mean PaCO₂ level also increased significantly before and after 60 min of hyperbaric treatment.

The RR, HR and BP of the volunteers at different altitudes are shown in Fig. 6. There were no significant differences in mean RR, HR and SBP/DBP before and after hyperbaric treatment at 355 m. At 2880 m, the mean RR after hyperbaric treatment was lower than before hyperbaric treatment, but the mean HR and SBP/DBP were not significantly different. At 4532 m, the mean RR and HR values after hyperbaric treatment were lower than before hyperbaric treatment, but the mean SBP/DBP values were not significantly different.

Changes in PaO₂ with increasing pressure inside the chamber at different altitudes are shown in Fig. 7 (B). PaO₂ was also progressively limited with increasing altitude, decreasing linearly by a factor proportional to the pressure inside the chamber.

4.3. Adverse events

Fortunately, we did not record any major adverse effects among inside observers. However, due to the changes in pressure, ear discomfort did occur in some volunteers.

5. Discussion

The purpose of this paper is to validate the effects of the new plateau hyperbaric chamber on alleviating high altitude hypoxia. Our results confirmed that the plateau hyperbaric chamber could increase the PaO₂ of rabbits and volunteers at higher gas densities of 355 m, 2880 m and 4532 m. Our results also show the increases in PaO₂ levels are broadly proportional to the fall in barometric pressure with increasing altitude. These measurements of arterial blood gases in rabbits and volunteers provide a picture of the pattern and limits of changes in rabbit and volunteer blood gases in response to hyperbaric treatment at different altitudes.

AMS occurs in approximately 10 to 25% of unacclimated persons who ascend to 2500 m and 50 to 85% of unacclimated persons at 4500 to 5500 m [10]. Considering the morbidity of AMS, we chose 2880 and 4532 m as the locations for test sessions. However, risk assessment of rabbits and human trials should be performed at 355 m.

In the rabbit study, we found that the mean PaO₂ level of experimental group rabbits increased significantly after 60 min of hyperbaric treatment at each altitude. However, the mean PaO₂ level of control group rabbits also increased significantly after 60 min of exposure to room air at each altitude. However, by comparing the mean PaO₂ levels after 60 min of intervention (hyperbaric treatment or exposure to room air), the mean PaO₂ level of experimental group rabbits was higher than the mean PaO₂ level of the control group at each altitude. We

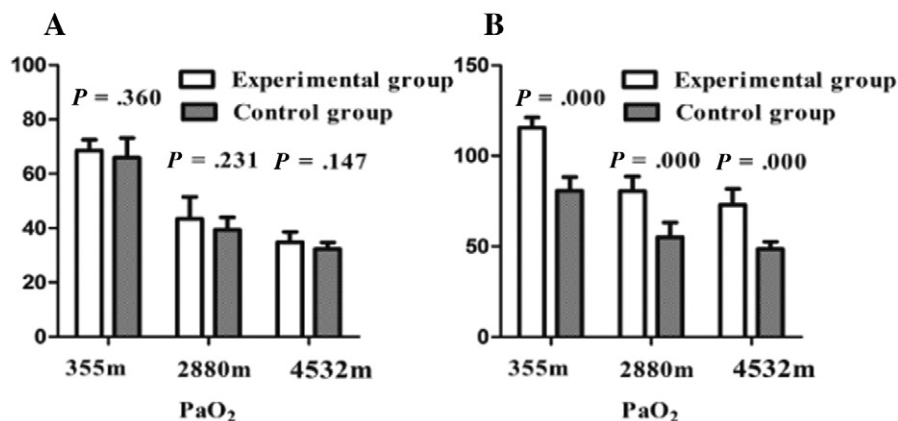


Fig. 5. PaO₂ levels of experimental and control group rabbits were analyzed before and after intervention to evaluate the influence of tracheal intubation on PaO₂. (A) Before the intervention, the mean PaO₂ levels of the two groups were not different at each altitude. (B) The mean PaO₂ levels of the experimental group were higher than those of the control group at each altitude.

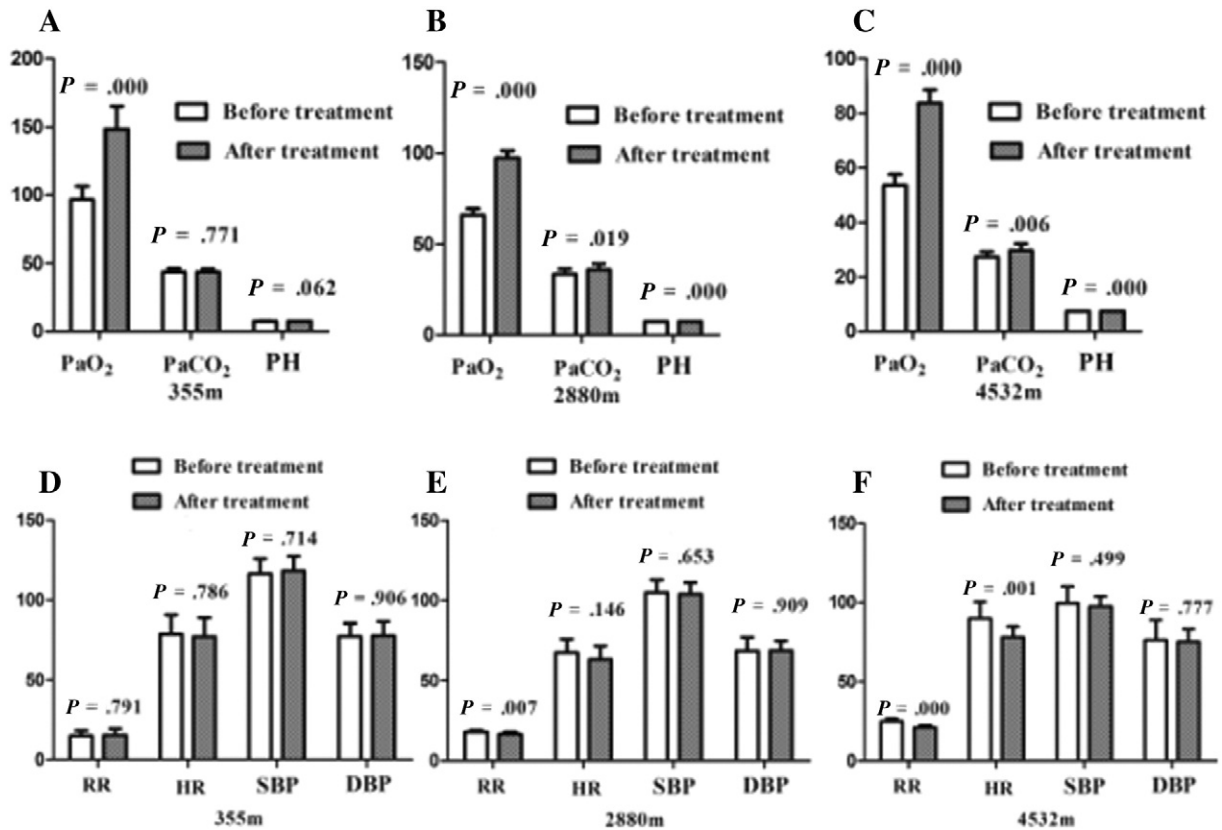


Fig. 6. The arterial blood gas analysis results (PaO₂, PaCO₂ and pH), RR, HR and BP of volunteers at different altitudes: (A, D) At 355 m, after 60 min of hyperbaric treatment, the mean PaO₂ level rose from 96.38 ± 9.80 to 148.38 ± 16.94 mmHg ($t = 19.036$, $P = 0.000$), the mean PaCO₂ level rose from 43.78 ± 2.66 to 43.83 ± 2.00 mmHg ($t = -0.297$, $P = 0.771$), the mean pH fell from 7.39 ± 0.16 to 7.37 ± 0.02 ($t = 2.024$, $P = 0.062$), RR rose from 14.88 ± 3.36 to 15.38 ± 4.03 /min ($t = -0.270$, $P = 0.791$), HR fell from 78.88 ± 11.69 to 77.25 ± 11.84 /min ($t = -0.374$, $P = 0.714$), SBP rose from 116.50 ± 9.43 to 118.25 ± 9.29 mmHg ($t = -0.374$, $P = 0.714$), and DBP rose from 77.50 ± 7.98 to 78.00 ± 8.62 mmHg ($t = -0.120$, $P = 0.906$). (B, E) At 2880 m, after 60 min of hyperbaric treatment, the mean PaO₂ level rose from 66.24 ± 3.33 to 97.29 ± 4.16 mmHg ($t = -24.025$, $P = 0.000$), the mean PaCO₂ level rose from 33.53 ± 2.90 to 36.12 ± 3.20 mmHg ($t = -2.473$, $P = 0.019$), the mean pH fell from 7.43 ± 0.01 to 7.41 ± 0.02 ($t = 4.743$, $P = 0.000$), RR fell from 17.88 ± 1.17 to 16.53 ± 1.55 /min ($t = -2.881$, $P = 0.007$), HR fell from 67.82 ± 8.26 to 63.59 ± 8.31 /min ($t = 1.490$, $P = 0.146$), SBP fell from 105.12 ± 7.78 to 103.94 ± 7.33 mmHg ($t = 0.454$, $P = 0.653$), and DBP rose from 68.82 ± 8.65 to 69.12 ± 6.00 mmHg ($t = -0.115$, $P = 0.909$). (C, F) At 4532 m, after 60 min of hyperbaric treatment, the mean PaO₂ level rose from 53.44 ± 4.07 to 83.81 ± 4.87 mmHg ($t = -19.141$, $P = 0.000$), the mean PaCO₂ level rose from 27.38 ± 1.82 to 29.69 ± 2.52 mmHg ($t = -2.973$, $P = 0.006$), the mean pH fell from 7.45 ± 0.02 to 7.43 ± 0.02 ($t = 4.044$, $P = 0.000$), RR fell from 24.88 ± 1.78 to 21.13 ± 1.45 /min ($t = 6.516$, $P = 0.000$), HR fell from 89.75 ± 10.61 to 78.31 ± 6.68 /min ($t = 3.649$, $P = 0.001$), SBP fell from 99.38 ± 10.53 to 97.25 ± 6.61 mmHg ($t = 0.684$, $P = 0.499$), and DBP rose from 76.38 ± 12.44 to 75.31 ± 8.10 mmHg ($t = 0.286$, $P = 0.777$).

think that this probably reflected the effects of endotracheal intubation. During the experiment, the rabbits were anesthetized. Thus, heart rate and blood pressure were not monitored.

Considering the changes in rabbit blood pressure and the physical factors of volunteers, we did not collect 3 arterial blood samples (0, 30, 60 min) at each altitude as originally planned.

However, in the human study, HR, RR and BP were monitored during hyperbaric treatment to evaluate the impact of the plateau hyperbaric chamber on the human body. Our results confirmed that this hyperbaric treatment has possible beneficial psychological effects on HR and RR at 2880 and 4532 m and has little effect on blood pressure at 355, 2880 and 4532 m.

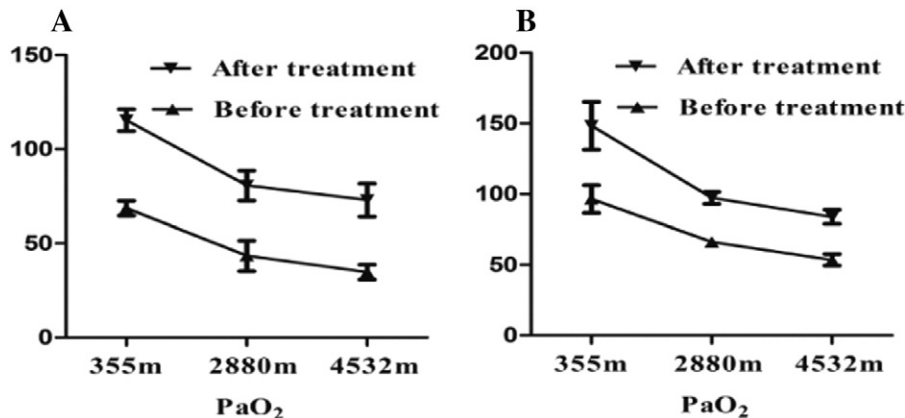


Fig. 7. Changes in PaO₂ with increasing pressure inside the chamber at different altitudes. (A) Animal experiments, (B) Human experiments. As predicted, PaO₂ was progressively limited with increasing altitude, decreasing linearly by a factor proportional to the pressure inside the chamber.

Intriguingly, at 2880 m and 4532 m, when the mean PaO₂ level was significantly increased, the mean PaCO₂ level also significantly increased before and after 60 min of hyperbaric treatment. This may be explained by the fact that RR of volunteers lower after hyperbaric treatment. One reason is respiratory compensation for hypoxia: when the volunteers are in the hypoxic environment, the frequency of breathing increasing. Nevertheless, the PaO₂ of volunteers will be increased during hyperbaric treatment, and a higher level of PaO₂ could protect cardiopulmonary function. Another reason may be that volunteers were in a quiet state during hyperbaric treatment, so the RR lower than movement state.

5.1. Limitations

However, several questions remain. First, in our study, arterial blood samples were analyzed using the i-STAT 200 blood gas analyzer and the G3⁺ Blood gas slice, which does not evaluate blood lactate concentration or oxygen saturation (SaO₂). Thus, the blood lactate and SaO₂ were not analyzed. Second, because all volunteers were healthy people, we could not determine any notable long-term beneficial or adverse effects associated with this treatment. Finally, the most important limitation is that the value of the new multiplace plateau hyperbaric chamber for treating AMS was not confirmed in field conditions.

5.2. Conclusions

From our findings, we can confirm that the new multiplace plateau hyperbaric chamber can be used to alleviate plateau hypoxia by increas-

ing patient PaO₂. However, the value of the chamber for treating AMS must be confirmed in field conditions.

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