四川大学学报（医学版） 2024，55（6）：1501－1506
J Sichuan Univ（Med Sci）

在线全文

平原低氧模拟环境适应不良对急性高原病发病的预警研究*

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【摘要】 目的 观察入高原前于平原吸入低氧发生器产生的低氧气体后受试者症状及相关生理指标改变，探索其对受试者进入高原后急性高原病（acute mountain sickness，AMS）的预警作用。**方法** 选择拟进高原人员50人，男性，平均年龄（22.00±1.52）岁，持续吸入低氧发生器产生的低氧气体（模拟海拔高度5 200 m，氧气体积分数为10.80%）30 min，期间观察记录指端氧饱和度、心率、血压及不适症状。受试者进入4 020 m高原后第4天填写急性轻症高原病（acute mild altitude disease，AMAD）症状评分。受试者在平原进行低氧吸入时根据是否出现不适症状（包括嗜睡、头昏、胸闷、手厥冷出汗等）分为适应不良组（18例）和适应良好组（32例）；在进入高原后根据是否发生AMS分为发病组（28例）及未发病组（22例）。主要指标为AMS的发病率，包括AMAD和急性重型高原病（severe acute mountain sickness，SAMS）的发病率，适应不良组和适应良好组进入高原后的AMS发病率。次要指标为平原吸入低氧后指端氧饱和度变化与AMS发病、AMAD症状评分的关系。**结果** 50名受试者同时乘坐飞机进入目标海拔4 020 m高原，AMS发病率为56.0%（28/50），其中AMAD发病率为54.0%（27/50），SAMS发病率为2.0%（1/50），该重型病例为高原肺水肿。适应不良组和适应良好组进入高原后AMS发病率分别为88.9%（16/18）和37.5%（12/32），差异有统计学意义（P<0.01）。50例受试者于平原吸入低氧后在前11 min内指端氧饱和度均快速下降，发病组较未发病组下降更为明显，第5、第9及第11分钟组间差异有统计学意义（P<0.05）；50例受试者于第12～30分钟指端氧饱和度处于平台期，发病组与未发病组差异无明显区别。50例受试者平原低氧气体吸入30 min内指端氧饱和度均值与进高原后AMAD症状评分呈负相关（r=－0.300）。**结论** 平原吸入低氧气体后出现不适症状者更容易发生AMS，应警惕前11 min发生指端氧饱和度下降的情况。

【关键词】 急性高原病 低氧环境 适应不良 预警 指端氧饱和度

Early Warning Effect of Maladaptation to Simulated Hypoxic Conditions at Low Altitudes for the Onset of Acute Mountain Sickness

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【Abstract】 Objective To observe the changes in the symptoms and relevant physiological indicators in subjects after inhaling the hypoxic air produced by a hypoxic air generator at a low altitude prior to their entry into high-altitude environment, and to explore its early warning effect for acute mountain sickness (AMS) among the subjects upon their subsequent entry into high-altitude environment. **Methods** A total of 50 subjects who were going to visit high-altitude regions were enrolled. All subjects were men, with an average age of (22.00±1.52) years. They continuously inhaled for 30 minutes hypoxic air (which simulated the air at the altitude of 5 200 m, with an oxygen content 10.80%) generated by a hypoxic air generator. During this period fingertip oxygen saturation, heart rate, blood pressure, and symptoms of discomfort were observed and recorded. On the fourth day after living at an altitude of 4 020 m, the subjects completed the evaluation for the symptom scores of acute mild altitude disease (AMAD). The subjects were divided into a maladjusted group (18 cases) and a well-adjusted group (32 cases) according to whether they experienced discomfort (including drowsiness, dizziness, chest tightness, cold sweating of the hands, etc.) during the inhalation of hypoxic air at a low altitude. After entry into the high-altitude environment, they were divided into an AMS group (28 cases) and a non-AMS group (22 cases) according to whether they experienced AMS after entering the he high-altitude environment. The primary indicator was the incidence of AMS, including the incidence of AMAD and severe acute mountain sickness (SAMS), and the incidence of AMS in the maladjusted group and the well-adjusted group after entering high-altitude environment. The secondary indicator was the relationship between the changes in fingertip oxygen saturation after inhaling hypoxic air at a low altitude and the incidence of AMS and the AMAD symptom scores. **Results** All 50 subjects traveled by air to the target altitude of 4 020 m above sea level at the same time. The AMS incidence among them was 56.0% (28/50), with the incidence of AMAD being 54.0% (27/50) and the incidence of SAMS being 2.0% (1/50). In the

* 西藏自治区重大课题（No. XZ202201ZD0001G02）资助

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出版日期：2024-11-20

single case of SAMS, the patient had high-altitude pulmonary edema. The incidences of AMS after entering high-altitude environment in the maladjusted and well-adjusted groups were 88.9% (16/18) and 37.5% (12/32), respectively, and the difference was statistically significant (P<0.01). In the 50 subjects, fingertip oxygen saturation decreased rapidly in the first 11 minutes into the inhalation of hypoxic air at a low altitude, with a more pronounced decrease in the AMS group than that in the non-AMS group, and the differences between the groups were statistically significant after 5, 9, and 11 minutes (P<0.05). Fingertip oxygen saturation plateaued in the 50 subjects from the 12th to the 30th minute, with no significant differences between the AMS and non-AMS groups. The mean value of fingertip oxygen saturation within 30 minutes of hypoxic air inhalation was negatively correlated with the AMAD symptom scores after subjects' entry into high-altitude environment (r=—0.300). **Conclusion** Those who experience symptoms of discomfort after exposure to hypoxic air produced by a hypoxic air generator at a low altitude are more likely to develop AMS and close attention should be paid to the decrease in fingertip oxygen saturation within the first 11 minutes.

【**Key words**】 Acute mountain sickness Hypoxic environment Maladaptation Early warning Fingertip oxygen saturation

人体急进高原后由于急性缺氧引起的多系统紊乱称为急性高原病(acute mountain sickness, AMS)[1]。AMS发病率在海拔3 000 m地区为56.47%, 在海拔4 520 m高原则高达95.55%[2]。急性轻型高原病(也称急性高原反应, acute mild altitude disease, AMAD)若得不到及时治疗可能进展为急性重型高原病(severe acute mountain sickness, SAMS)[3], 对进高原人群的生命安全构成极大的威胁[4-5]。随着我国高原地区的快速发展, 因经济、旅游、文化交流、军事等由平原地区乘坐多种交通工具快速进入高原地区的人群不断增加, 迫切需要对AMS精准预测、精准预防、预前处置、减少发病率及病死率。已有机构通过系统预防, 将AMS发病率降到5%以下[5]。降低AMS发病率的关键之一在于预测, 并对预测出的高危发病个体进行专业预防及早期处置。本研究采用低氧发生器在平原模拟高原低氧环境对AMS发病的预测进行了探索, 对预防、预警AMS及防止AMAD进一步恶化具有重要意义。

1 资料与方法

1.1 对象资料

纳入标准: 男性; 18 ~ 30岁; 体质量指数18.5 ~ 23.9 kg/m^2; 长期生活在低海拔地区, 且近3个月内未至海拔≥2 500 m高原地区; 顺利于重庆通过健康体检(以下体检内容均未见异常: 血常规、肝肾功能、血脂、血糖、普通心电图、胸部X射线、腹部B超、内外科体格检查); 既往无循环、呼吸、消化、血液、泌尿、神经或其他系统慢性病史, 无肺结核或乙型肝炎等传染病史; 既往无急、慢性高原病史; 近2周内无呼吸道及消化道急性病史; 具有完全民事行为能力, 自愿入组并签署知情同意书; 未参加其他实验并能全程配合参与本次实验。不符合上述情况之一者则排除此次实验。本研究经西藏军区总医院医学伦理委员会审核批准, 批准号: 2021XZZYYKY-010。

最终纳入拟进高原人员50例男性, 平均年龄(22.00±1.52)岁。

1.2 方法

1.2.1 测量指标

受试者经身高、体质量、指端氧饱和度、心率、血压检测后, 在重庆(海拔240 m)于进高原前1周内进行低氧发生器低氧气体吸入实验。低氧发生器型号为美国Higherpeak公司生产的“Denali MAG-30Altitude Generator”, 将低氧发生器调整至效应海拔5 200 m, 产生低氧气体(氧气体积分数10.80%)。运用专用面罩吸入10.80%低氧气体30 min, 使用“YX301 yuwwell”指夹式脉搏血氧仪连续监测心率、指端氧饱和度(统一测右手食指, 测量前注意手部保暖), 每分钟记录测量结果1次。同时记录受试者有无不适症状。

受试者由重庆乘飞机进入海拔4 020 m高原, 进入高原后每日仅进行一般日常体力活动, 第4天在西藏军区总医院高山病科专科医师指导下, 根据受试者个人症状填写急性高原反应症状评分(AMAD症状评分)[6]。该评分包括了主要症状(头痛、呕吐)及其他症状(头昏、恶心、心悸、气短、胸闷、眼花、食欲不振、失眠、腹胀、腹泻、便秘、口唇发绀、四肢麻木及嗜睡), 根据严重程度分为头痛: 2 ~ 7分, 呕吐: 2 ~ 7分, 其他症状每出现一个记1分; 总分1 ~ 4分为基本正常, 5 ~ 10分为轻度, 11 ~ 15分为中度, ≥16分则为重度。若评分≥16分或出现高原肺水肿(high altitude pulmonary edema, HAPE)或高原脑水肿(high altitude cerebral edema, HACE)者立即送医院诊治。

1.2.2 术语定义和标准

本研究中AMS(包括AMAD、SAMS)诊断标准采用中华人民共和国国家军用标准(GJB1098A—2022)。该AMS的诊断标准主要基于临床症状(病史和体格检查),

通常不需要实验室检查,有助于医疗工作者在高原地区快速识别和处理AMS。

AMAD诊断标准: ①机体近期由平原快速进入海拔2 500 m以上高原,或由高原进入更高海拔地区,在数小时或1 ~ 3 d内发病; ②有头痛、头昏、恶心、呕吐、心慌、气短、胸闷、胸痛、失眠、嗜睡、食欲减退、腹胀、手足发麻等不适症状之一或以上(且AMAD症状评分≥5分),或有静息时脉搏显著增快、血压轻度或中度升高(也可偏低)、口唇及(或)手指发绀、眼睑或面部水肿等体征之一或以上,且经检查不能用其他原因解释者; ③ 3 ~ 5 d内或采取吸氧、转入低处等措施后上述症状或体征即减轻或恢复。上述3个条件必须同时满足方可诊断。

HAPE现场诊断标准: ①近期由平原快速进入海拔2 500 m以上高原,或由高原进入更高海拔地区; ②症状: 静息时呼吸困难,胸闷压塞感,平卧时咳嗽显著、咳白色或粉红色泡沫样痰,无力或活动能力减低; 体征: 中央性紫绀,一侧或双侧肺野出现湿啰音或喘鸣音、呼吸过速、心动过速。满足第1条基础上,症状、体征至少各具2项时可做出诊断。

HACE现场诊断标准: ①近期由平原快速进入海拔2500 m以上高原,或由高原进入更高海拔地区; ②AMAD症状评分≥5分且出现神经精神状态改变和(或)共济失调,或AMAD症状评分< 5分但同时出现神经精神状态改变及共济失调(神经精神症状按程度依次为冷漠/倦怠、定向障碍/精神错乱、昏睡/昏迷; 共济失调按程度分为平衡技巧失调、步幅出线、跌倒、不能站立)。必须同时满足上述2个条件方可诊断。

HAPE及HACE均为SAMS。

1.2.3　分组

50例受试者在平原进行低氧吸入时根据是否出现不适症状(包括嗜睡、头昏、胸闷、手厥冷出汗等)分为适应不良组和适应良好组。在进入高原后根据是否发生AMS进行分组,分为发病组及未发病组。

1.2.4　结局指标

1.2.4.1　主要指标

AMS发病率: 可直接反映研究干预措施对预防AMS的效果。包括AMAD和SAMS的发病率,适应不良组和适应良好组进入高原后的AMS发病率。

1.2.4.2　次要指标

指端氧饱和度的变化: 吸入低氧气体时指端氧饱和度的变化与AMS发病、AMAD症状评分的关系。

1.2.5　统计学方法

数据采用SPSS 23.0及R 4.4.1软件进行分析。计量资料以$\bar{x} \pm s$表示,组间比较采用t检验; 计数资料以频数或百分率表示,组间比较选用χ^2检验。衡量两个连续变量的线性关系用Pearson相关系数。P< 0.05为差异有统计学意义。

2　结果

2.1　AMS发病情况

50例受试者同时乘坐飞机进入目标海拔4 020 m高原,AMS发病率为56.0%(28/50),其中AMAD发病率54.0%(27/50), SAMS发病率为2.0%(1/50),该例为HAPE,未出现HACE病例(0/50)。

2.2　平原低氧气体吸入时出现不适症状与进入高原后的AMS发病情况

见表1。适应不良组共18例,适应良好组共32例,两组进入高原后AMS发病率分别为88.89%(16/18)和37.50%(12/32),差异有统计学意义(P< 0.01)。

2.3　平原低氧气体吸入时指端氧饱和度改变与AMS发病关系

2.3.1　平原吸入时低氧气体指端氧饱和度变化趋势

50例受试者在平原时,持续低氧气体吸入后第1 ~

表 1　50例受试者进入高原后AMS发病情况

Table 1　AMS morbidity after entry into high-altitude environment in the 50 subjects

In plains	After entering high-altitude environment				
Symptoms of inhalation of hypoxic	AMAD/case	SAMS/case		AMS in total[#]/case (%)	Without AMS/case
		HAPE	HACE		
Symptomatic group (n=18)	15	1	0	16 (88.89)	2
Drowsiness (n=5)	3	0	0	–	2
Dizziness (n=5)	5	0	0	–	0
Blurred vision (n=1)	0	1	0	–	0
The compound symptoms[*] (n=7)	7	0	0	–	0
Asymptomatic group (n=32)	12	0	0	12 (37.50)	20

AMAD: acute mild altitude disease; AMS: acute mountain sickness; SAMS: severe acute mountain sickness; HAPE: high altitude pulmonary edema; HACE: high altitude cerebral edema. [*] The compound symptoms are defined as having two or more of the follwing symptoms, drowsiness, dizziness, chest tightness, cold hands, syncope, and sweating. [#] Only calculate the totals of symptomatic group and asymptomatic group.

11 分钟氧饱和度较快下降,第12 ~ 30分钟下降不明显,处于平台期。见图1A。

进入高原后AMS发病组28例,未发病组22例。在平原吸入低氧气体时的氧饱和度进行比较,前20 min发病组氧饱和度均值均低于未发病组;第21 ~ 30分钟两组氧饱和度值接近。其中平原吸入低氧第5、第9及第11分钟,发病组与未发病组氧饱和度相比降低,经t检验,组间差异有统计学意义($P<0.05$)。见图1B。

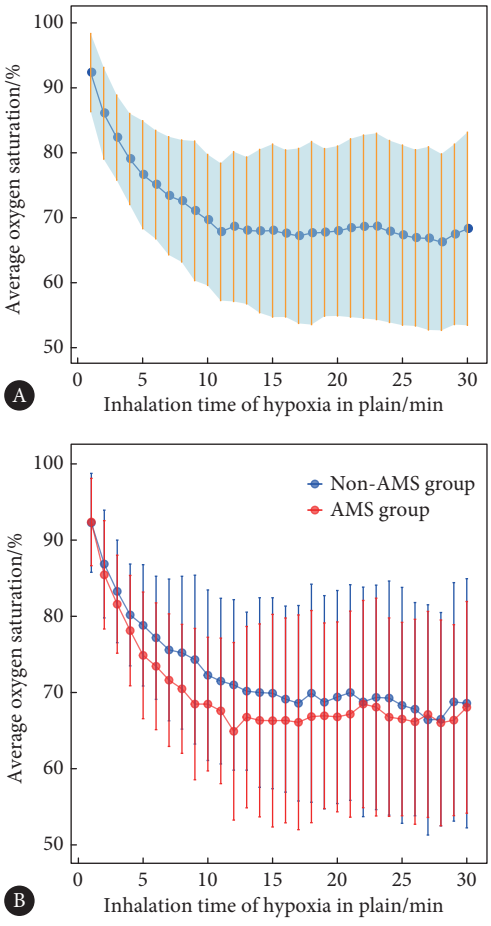

图 1 平原吸入低氧气体后指端氧饱和度变化曲线

Fig 1 Changes in fingertip oxygen saturation after inhaling hypoxic air at a low altitude

A, Overall trend (n=50), with the shaded areas indicating standard deviation ranges. B, comparison between the AMS group (n=28) and the non-AMS group (n=22).

2.3.2 平原低氧气体吸入30 min内指端氧饱和度均值与进高原后AMAD症状评分分值的关系

50例受试者,进高原后第4天AMAD症状评分结果:1 ~ 4分22例,轻度(5 ~ 10分)23例,中度(11 ~ 15分)4例,重度(≥16分)1例。平原低氧气体吸入30 min内指端氧饱和度均值与进高原后AMAD症状评分呈弱的负相关(r= —0.300, P= 0.033 98)。见图2。

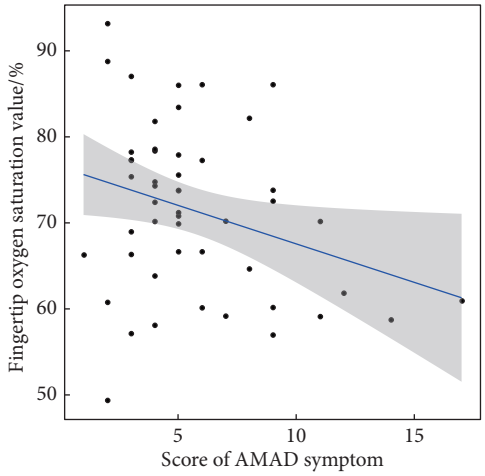

图 2 吸入低氧气体30 min内指端氧饱和度均值与AMAD症状评分分值散点图(Pearson相关)

Fig 2 Scatter diagram with 95% confidence interval of mean fingertip oxygen saturation and AMAD symptom scores in the 30 minutes of inhalation of hypoxic air (Pearson correlation)

Y= —0.100 638X+12.846 389. R^2=0.09, r= —0.300, 95% confidence interval (—0.534, —0.024) (Gray area), P=0.033 98.

3 讨论

AMS发病受多因素影响且存在人群及个体易感性,其他研究者曾采取多样化的模拟方法进行预测和探索[7-14],常用模拟方法有低压氧舱法[15]及常压低氧房法,缺点是场地固化、不易社会推广及大批量人员测试,且模拟海拔高度不易控制。本研究采用低氧发生器配合专用面罩,模拟海拔高度可调,设备轻便、易搬动,受试者常处于静坐状态,安全可保证,生理指标易监测。通过实验,发现指端氧饱和度与AMS关联症状可能是预测AMS发病的关键指标。

本研究提示应注意平原吸入低氧气体11 min内的氧饱和度。人体进入高原低氧环境后,通过增加呼吸摄氧、心输出量、无氧代谢,血液重分布,激活抗缺氧基因等对抗缺氧,因而本研究从缺氧指标如动脉血氧分压、指端氧饱和度(该两者有密切相关性[16])中选择了便捷、无创、易于连续动态观测的后者来观测。本研究结果提示,50例受试者于平原开始吸入低氧气体(模拟海拔5 200 m)的前11 min内氧饱和度均快速下降,且AMS发病组指端氧饱和度下降程度较未发病组更为明显,甚至在第5分钟即可表现出差异有统计学意义,提示吸入低氧时指端氧饱和度下降明显者对抗缺氧及代偿能力弱、易发生AMS,提示平原吸入低氧气体后11 min内(甚至第5分钟)的氧饱和度或可成为预测AMS发病的关键指标。

本研究表明,在平原吸入低氧后出现嗜睡犯困、头

昏、胸闷、手冷厥出汗及视力模糊这些不适症状者更有可能出现AMS发病。不适症状在实验完成后1 min内即刻消失，实验安全可控，或可作为预警AMS发病关键指标。

本研究发现平原吸入低氧气体30 min内指端氧饱和度均值与进高原后AMAD症状评分呈弱负相关。这一发现对于更深理解AMS的发病机制具有重要意义，它强调了在低氧环境下，氧饱和度对于评估个体对高原环境适应性的关键性[17]。虽然这一现象对AMS的预测、预防提供了新的视角，但这次结果仅为弱负相关，还需要进一步的研究来验证其普适性和作用机制。未来还需扩大实验人数，在保证受试者安全的前提下可适当增加模拟频次或延长模拟时间，以明确上述两者是否存在更强的相关性。

本次研究的目的就是为寻找更多的预测AMS的敏感指标，从而完善预测体系，而此次结果也已初步证明在平原运用低氧发生器模拟高原缺氧环境可能在未来会成为一种积极且有效的方法。

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作者贡献声明　柏雪烨紫负责论文构思、正式分析、调查研究、研究方法、初稿写作和审读与编辑写作，黄学文负责调查研究和研究项目管理，马海林负责提供资源和监督指导，李尚师负责数据审编和审读与编辑写作，李茂仕负责数据审编和研究方法，孙学文、王授衔、高文文、张文皓、刘慕源和杨宇负责正式分析和调查研究。所有作者已经同意将文章提交给本刊，且对将要发表的版本进行最终定稿，并同意对工作的所有方面负责。

Author Contribution　BAI Xueyezi is responsible for conceptualization, formal analysis, investigation, methodology, writing--original draft, and writing--review and editing. HUANG Xuewen is responsible for investigation and project administration. MA Hailin is responsible for resources and supervision. LI Shangshi is responsible for data curation and writing--review and editing. LI Maoshi is responsible for data curation and methodology. SUN Xuewen, WANG Shouxian, GAO Wenwen, ZHANG Wenhao, LIU Muyuan, and YANG Yu are responsible for formal analysis and investigation. All authors have agreed to submit articles to this journal, and finalize the version to be published, and agree to be responsible for all aspects of the work.

利益冲突　所有作者均声明不存在利益冲突

Declaration of Conflicting Interests　All authors declare no competing interests.

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(2024 – 07 – 31收稿, 2024 – 10 – 08修回)

编辑 吕 熙