A Dynamic Rabbit Model of Sinus Barotrauma and Its Related Pathology

Xianrong Xu; Binru Wang; Zhanguo Jin; Yang Zhang

BACKGROUND: This study was undertaken to establish a dynamic animal model of sinus barotrauma (SB).

METHODS: The right nasal cavities of 65 rabbits were filled with sponges to obstruct the right ostiomeatal complex (OMC), while in the left nasal cavities, the left OMC was kept clear. The rabbits were exposed to hypobaric chamber simulation. The right sinuses were assigned as the model group, randomly divided into 13 subgroups with 5 in each subgroup, while the left sinuses were assigned as the control group. The hypobaric chamber simulation involved 6 pairs of ascending/descending speeds (100 $m \cdot s^{-1}$, 75 $m \cdot s^{-1}$, 50 $m \cdot s^{-1}$) to 2 altitudes (13,123 ft or 6562 ft). The ascending/descending speed for Model Group 13 was 15 $m \cdot s^{-1}$ to an altitude of 13,123 ft. The control group was not exposed to hypobaric chamber simulation or obstruction of the OMC. All rabbits were monitored for behavior and via nasal endoscopy, MRI, and mucosal pathology, and statistically analyzed.

RESULTS: SB appeared at the ascending/descending speeds of 50 $m \cdot s^{-1}$, 75 $m \cdot s^{-1}$, and 100 $m \cdot s^{-1}$. SB was more obvious at 100 $m \cdot s^{-1}$ than at 50 $m \cdot s^{-1}$ and 75 $m \cdot s^{-1}$, and SB happened mainly at altitudes between 0-6562 ft. Based on behavior during hypobaric chamber simulation and the results of endoscopic morphology, imaging, and cell pathology, SB could be divided into mild, moderate, and severe.

DISCUSSION: By obstructing the OMC and using hypobaric chamber simulation at high ascending/descending speeds and altitude, a dynamic rabbit model of SB at various degrees was established. The severity of SB was proportional to the ascending/descending speeds and mainly seen below 6562 ft.

KEYWORDS: disease models, animal, rabbits, hypobaric chamber simulation.

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Sinus barotrauma (SB) is acute sinus mucosal lesions induced by compressed air in the sinus when the outside air (or water) pressure suddenly changes. SB occurring in the aviation environment is called aero-sinusitis. Symptoms of SB, when severe, include blurred vision, difficulties in oxygen inhalation from a mask, severe pain, and even shock, which could affect aerial work and endanger flight safety.[7,8] SB occurs not only in professional flight crew, parachutists, and divers, but also in airline passengers, high-speed car passengers, and flight and diving enthusiasts.[12,15,25] As a common disease in aviation medicine, SB is ranked second in hospitalizations for nasal disease and fifth in physical examination findings of nasal diseases for flight personnel.[18] It is also ranked fourth in hospitalizations for otorhinolaryngology diseases for fighter pilots.[17] The incidence of SB ranges from 1.5 to 44.0% for pilots in hypobaric chamber simulations.[2] Rosenkvist and others surveyed 948 cases of Danish civil aviation pilots, and found about 12% of pilots had had SB, about 70–80% of which was frontal sinus barotrauma.[13] The clinical symptoms have been thoroughly investigated. However, the elimination and detection rates of sinus pressure dysfunction are very low in the physical examination of cadets and the annual physical examinations of pilots, possibly owing to imperfection in SB characterization, detection methods, and evaluation criteria.[18,24] In this study, we established a dynamic SB model with ostiomeatal complex (OMC) obstruction and hypobaric chamber simulation at

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different ascending/descending speeds and altitudes to investigate its dynamic pathogenesis, characteristics, morphology, imaging and histopathology, grading standards, and objective qualitative and quantitative testing methods, with the hope of providing references for SB's medical evaluation, prevention, and control.

METHODS

Subjects

Beijing Fangshan Guandaoshunli Farm provided 70 healthy, male adult Japanese white rabbits weighing 2500-3000 g. They had unobstructed nasal cavities and no sneezing, nasal congestion, nasal bleeding, or watery, inflammatory, or bloody discharge. After 2 wk of accommodation in a standard animal room, the experiment was started and the animals were given food and water ad libitum. The experiments were approved by the Institutional Animal Care and Use Committee (IACUC) of the General Hospital of the PLA Air Force.

Equipment

The items used were 5% ketamine (0.5 ml $\cdot$ kg^{-1}), complex Sumianxin II (0.5 ml $\cdot$ kg^{-1}), 1% povidone-iodine disinfectant, 2% lidocaine, and Merocel high expansion hemostatic sponges (Medtronic, Minneapolis, MN). A sinus endoscope with a diameter of 3 mm and visual angle of 0°, and a functional sinus endoscopic system (Storz Inc., Tuttlingen, Germany), and an Olympus optical microscope were also used. The hypobaric chamber (CGK-48M) was from the Center of Clinical Aviation Medicine, PLA, General Hospital of Air Force, Beijing, China. The MRI with a matrix of 384 $\times$ 256, an FOV of 18 cm $\times$ 18 cm, gradient field strength of 45 mT $\cdot$ m^{-1}, and a maximum switching rate of 200 mT $\cdot$ m^{-1} $\cdot$ s^{-1} was a Magenetomessenza from Siemens (Erlangen, Germany).

Procedures

There were five randomly selected rabbits that were put under general anesthesia with an intramuscular injection of ketamine complex Sumianxin II into the gluteus maximus. A longitudinal incision was made in the nasal cavity slightly left to the midline to fully expose the right nasal cavity. The anatomy of rabbit nasal sinuses and adjacent relationships were observed. The vertical length, inner and outer diameters of the nostril, and vertical distance of the anterior nostril to the rear maxillary sinus ostium were measured to be 5.10 $\pm$ 0.23 mm, 2.50 $\pm$ 0.21 mm, and 29.04 $\pm$ 0.75 mm, respectively. In addition, bilateral sinus mucosal specimens were obtained for pathological examination. Based on the measurement results, the expansion sponge was prepared to be 5.0 $\times$ 2.5 $\times$ 30.0 mm to obstruct the OMC.

The right nasal cavities of 65 rabbits were filled with prepared expansion sponges to obstruct the right OMC, while the left nasal cavity was not filled and the left OMC was kept clear. The 65 rabbits were then exposed to hypobaric chamber simulation. The left sinuses were assigned to be the control group, while the right sinuses were assigned to be the model group, which were randomly divided into 13 subgroups with 5 in each subgroup. The remaining five rabbits were assigned as a blank control group and placed in the hypobaric chamber for the same period as during the hypobaric chamber simulation, but not exposed to the ascending/descending procedures. The rabbits were put in the prone position and fixed on the animal operating table under general anesthesia. After disinfecting the external nostrils (about 2.5 cm in diameter) with iodine, two drops of a mixture (1:1, v/v) of 2% lidocaine and 1% furacilin were applied to each nasal cavity. The rabbits were subjected to nasal endoscopy 2 min later and two prepared sterile expansion sponges were placed in the right nasal cavity before they were injected with 0.5 ml of 0.9% sodium chloride to obstruct the OMC. Each rabbit was labeled, put in its cage, and closely observed for behavioral changes. Once fully awake, they were exposed to hypobaric chamber simulation.

Rabbits in the model group were placed in cages and exposed to hypobaric chamber simulation at different ascending/descending speeds and altitudes as listed in **Table I** three times with a 5-min interval after ascending and 15 min between two consecutive tests. Behavioral changes in the rabbits during the hypobaric chamber simulation at different altitudes and speeds were observed. In addition, rabbits in the control group were placed in the hypobaric chamber for the same period of time, but not exposed to hypobaric chamber simulation.

Before the hypobaric chamber simulation, the rabbits were examined with sinus endoscopy. Changes in their behavior were observed during the hypobaric chamber simulation. After the hypobaric chamber simulation, the expansion sponges were removed, and the rabbits underwent sinus endoscopy, MRI, and mucosal cell morphology examinations. Both the right and left nasal cavities of all rabbits in the model group and one rabbit in the control group were examined using MRI 5 h after the hypobaric chamber simulation. In brief, the rabbits were fully anesthetized, their gluteus maximus was scanned with nasopharynx neck coil MRI with a sequence of T_1WI axial scanning (SE, TR of 450 ms, TE of 10 ms, slice thickness of 3 mm, interlayer spacing of 1 mm, number of excitations of 4, matrix of 384 $\times$ 256, as well as field of view of 18 cm $\times$ 18 cm), and T_2WI axial scanning (TSE, TR of 5000 ms, TE of 104 ms, slice thickness

Table I. Assignment of Rabbits into Model Groups and Hypobaric Chamber Simulation Methods.

ASCENDING AND DESCENDING SPEEDS	ALTITUDE 13,123 FT	ALTITUDE 6562 FT
100 m $\cdot$ s^{-1}↑,15 m $\cdot$ s^{-1}↓	Subgroup 1	Subgroup 2
15 m $\cdot$ s^{-1}↑, 100 m $\cdot$ s^{-1}↓	Subgroup 3	Subgroup 4
75 m $\cdot$ s^{-1}↑, 15 m $\cdot$ s^{-1}↓	Subgroup 5	Subgroup 6
15 m $\cdot$ s^{-1}↑, 75 m $\cdot$ s^{-1}↓	Subgroup 7	Subgroup 8
50 m $\cdot$ s^{-1}↑, 15 m $\cdot$ s^{-1}↓	Subgroup 9	Subgroup 10
15 m $\cdot$ s^{-1}↑, 50 m $\cdot$ s^{-1}↓	Subgroup 11	Subgroup 12
15 m $\cdot$ s^{-1}↑, 15 m $\cdot$ s^{-1} ↓	Subgroup 13	—

Subgroup 1 ascended from sea level to 13,123 ft at the speed of 100 m $\cdot$ s^{-1}, stayed for 5 min, and then descended to sea level at the speed of 15 m $\cdot$ s^{-1}. The same process was repeated twice with a time interval of 15 min. Subgroups 2-13 were done in the same manner.

of 3 mm, interlayer spacing of 1 mm, number of excitations of 4, matrix of 384 × 256, and field of view of 18 cm × 18 cm). All images were transferred to a workstation for examination and measurement.

Right maxillary sinus tissues were removed, fixed in 10% formalin solution for 7 d, and decalcified with fresh 10% ethylene diamine tetra-acetic acid every day for 3 wk. After dehydration with graded ethanol and defatting with dehydrated xylene, they were embedded in paraffin, serially sectioned (axial plane) to 5 μm thickness, and stained with HE. Four intact and well stained sections from each sample were examined under an optical microscope with five randomly selected fields for histopathological analysis. Based on the pathological features seen under the light microscope, the degree of cilia missing was classified as mild if less than 5%, moderate if between 5% and 20%, and severe if greater than 20%. The degree of inflammatory cell infiltration in the glandular cavity was classified as mild if the infiltration was confined to the lower layer of epithelial cells, severe if involving most of the epithelial layer, and moderate if the infiltration was in between.[6] The three pathological parameters (cilia missing, inflammatory cell infiltration, and epithelium ulceration) were semiquantitatively graded as normal (−), mild (+), moderate (++), and severe (+++). Differences between the groups were analyzed with the Kruskal-Wallis rank sum test with SPSS 19.0, and $P < 0.05$ was considered statistically significant.

RESULTS

The behavioral changes of the rabbits during the hypobaric chamber simulation are listed in **Table II**. The rabbits in Subgroups 1-12 showed 10 different types of general behavior and 6 different types of transient typical behavioral changes during rapid ascent to the maximum altitude and descent to the ground (Table II). The general behaviors were swallowing, runny nose, sneezing, repeated blinking, weeping, scratching nose, breathing through the mouth, rapid breathing, repeated head-shaking, and loss of consciousness. The typical transient behaviors were circling, standing, grasping the cage, hitting the cage, scratching the face, and breathing with face up. Rabbits in Subgroups 1-4 showed the most typical behavioral changes. Rabbits in Subgroup 13 and the control group showed no typical transient SB performance.

Rabbits in Subgroup 13 showed nasal patency and no turbinate congestion before or after hypobaric chamber simulation (**Fig. 1A**). By contrast, the rabbits in Subgroups 1-12 showed right nasal turbinate congestion and edema of varying degrees, and even had a large amount of mucosal secretion (**Fig. 1B and C**). After the hypobaric chamber simulation, the rabbits in Subgroup 13 and the control group showed transparent nasal cavity and sinuses (**Fig. 2A**), while the rabbits in Subgroups 1-12 showed varying degrees of opacification in the right, but not the left maxillary and ethmoid sinuses (**Fig. 2B and C**). In addition, rabbits in the control group had no significant lesions (Fig. 2C).

Table II. Behavioral Changes of Rabbits in Each Subgroup During Hypobaric Chamber Simulation.

SUBGROUP (5 PER SUBGROUP)	CHANGES IN GENERAL BEHAVIOR										CHANGES IN TRANSIENT TYPICAL BEHAVIOR						
	SWALLOWING	RUNNY NOSE	SNEEZING	REPEATED BLINKING	WEEPING	SCRATCHING NOSE	MOUTH BREATHING	RAPID BREATHING	REPEATED HEAD-SHAKING	LOSS OF CONSCIOUSNESS	CIRCLING	STANDING	GRASPING CAGE	HITTING CAGE	SCRATCHING FACE	BREATHING WITH FACE UP	HEIGHT WHEN APPEARING (KM)
1	+	+	±	+	+	±	−	+	+	−	+	+	+	−	+	+	↑4
2	+	+	±	+	+	−	−	+	+	−	+	+	±	−	+	+	↑2
3	+	+	±	+	+	±	−	+	+	−	+	+	+	±	+	+	↓2
4	+	+	±	+	+	−	−	+	+	−	+	+	±	−	+	+	↓1
5	+	+	±	+	+	±	−	+	+	−	±	+	−	−	±	+	↑4
6	+	+	−	+	+	−	−	+	±	−	−	±	−	−	−	+	↑2
7	+	+	±	+	+	−	−	+	+	−	±	+	±	−	±	+	↓2
8	+	+	−	+	+	−	−	+	±	−	−	+	+	−	±	+	↓1
9	+	+	±	+	+	−	−	+	+	−	±	+	+	−	−	+	↑4
10	+	+	−	±	+	−	−	+	±	−	−	±	−	−	−	+	↑2
11	+	+	±	−	+	−	−	+	+	−	+	+	−	−	±	+	↓2
12	+	+	−	−	+	−	−	+	±	−	−	±	−	−	±	+	↓1
13	±	−	−	−	−	−	−	+	±	−	−	−	−	−	−	−	−
control	±	−	−	±	−	−	−	+	±	−	−	−	−	−	−	−	−

"+" indicates behavioral changes occurring in all rabbits in the group; "−" indicates no behavioral changes in all rabbits in the group; "±" indicates behavioral changes occurring in some rabbits in the group

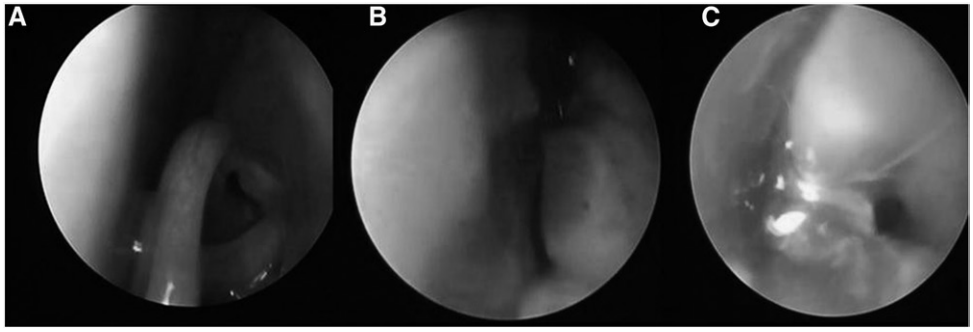

Fig. 1. Representative endoscopic images of rabbits in different subgroups. A) An endoscopic image of a rabbit showing normal structures and no turbinate congestion and nasal patency. B) An endoscopic image of a rabbit showing diffusive nasal mucosal congestion as well turbinate congestion and edema. C) An endoscopic image of a rabbit showing a large amount of watery or mucoid nasal discharge accompanied with nasal obstruction and an invisible sinus ostium structure.

After the hypobaric chamber simulation, the rabbits in Subgroup 13 and the control group showed no lesions in the maxillary sinus mucous membrane (**Fig. 3A**), while the rabbits in Subgroups 1-12 showed inflammatory changes in the maxillary sinus mucous membrane (**Fig. 3B and C**). The pathological changes in the sinus mucosa were quantitatively analyzed and the results are shown in **Table III**. Kruskal-Wallis rank sum test indicated that there were significant differences between Subgroups 1 and 5, 1 and 9, 2 and 6, 2 and 10, 3 and 7, 3 and 11, 4 and 8, 4 and 12, and between all Subgroups 1-12 and Subgroup 13 as well as the control group. Based on the symptoms and X-ray results, Campbell and Weissman graded SB into grades I, II, and III.[1,11,19] Referring to this grading system, we assumed pain by the behavior of the rabbits. SB degree in the rabbits was classified into mild, moderate, and severe, as shown in **Table IV**.

DISCUSSION

Based on the scientific theory of aviation rhinology, when sinus ostium congestion occurs, rapid ascent or descent during flight could easily lead to SB.[7,21,25] Clinically SB is often diagnosed based on symptoms, sinus CT or MRI, functional nasal endoscopy, and biopsy.[3,14,20] In this experiment, the OMC was obstructed and the rabbits were exposed to hypobaric chamber simulation at a variety of ascending and descending speeds and altitudes. After hypobaric chamber simulation, the rabbits' behavior, morphological changes in nasal endoscopy, MRI imaging, and cellular pathological indices were examined to establish a dynamic SB model. The design idea to establish the dynamic SB model is based on studying the dynamic relationship of SB at various ascending/descending speeds and altitudes, pathological lesion characteristics, detection methods, and grading standards. In detail, we observed whether SB appears in rabbits after being exposed to hypobaric chamber simulation at different ascending/descending speeds (100 $m \cdot s^{-1}$, 75 $m \cdot s^{-1}$, 50 $m \cdot s^{-1}$, or 15 $m \cdot s^{-1}$) and altitudes (13,123 ft or 6562 ft) based on the changes in behavior during the hypobaric chamber simulation, in sinonasal endoscopy, sinus CT or MRI, pathological indices of mucosal cells, etc. In more detail, we: 1) studied the occurrence of SB and its severity in model (right) sinuses and control (left) sinuses; 2) compared SB severity in rabbits after hypobaric chamber simulation at the same altitude, but four different ascending/descending speeds; 3) compared SB severity in rabbits after hypobaric chamber simulation at the same ascending/descending speeds, but two different altitudes; 4) provided the test basis of behavior, sinus morphology, and MRI imaging and pathology for SB rabbits; 5) collected the dynamic data of SB animals' behavior, endoscopy, imaging, and cell morphology and studied the SB dynamic mechanisms with focus on the cellular pathology; 6) conducted semiquantitative histopathological analysis of SB animals and performed objective quantitative research on SB; and 7) developed criteria for grading SB severity and conducted objective qualitative study on SB animals.

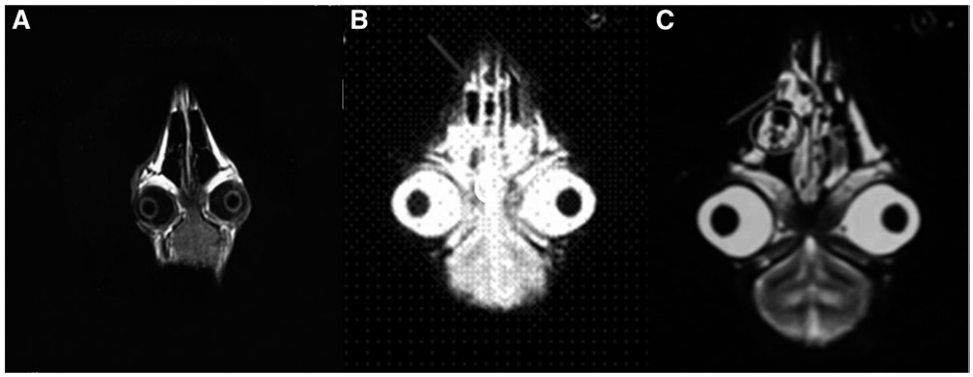

Fig. 2. Representative MRI images of rabbits in different subgroups. A) A MRI image showing smooth bilateral nasal cavity, clear maxillary and frontal sinuses, no abnormal discharges, and normal nasal mucosa. B) A MRI image showing discharge at the anterior maxillary sinus (arrow), cloudy nasal cavity, mucosal edema, exudation, and thickening at the right, but no obvious abnormalities at the left. C) A MRI image showing a high-density signal at the maxillary sinus, clear fluid level (arrow) in the nasal cavity, mucosal avulsion shadow (circle), extensive edema, and thickening of the nasal mucosa at the right, but no obvious abnormalities at the left.

Selecting appropriate animals is a key factor for successfully establishing the SB model. Japanese white rabbits have the following advantages and feasibility for SB modeling: 1) they are physically strong and gentle with strong disease resistance;[9] and 2) they have very similar nasal anatomic structures to those of humans. Their sinus cavity capacity is large and

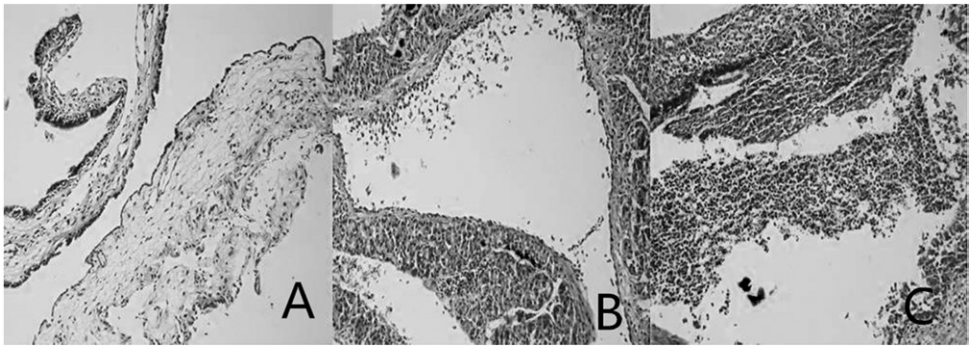

Fig. 3. Representative histopathological nasal cavity images of rabbits in different groups. A) A MRI image showing normal sinus mucosa. B) A MRI image showing more inflammatory cells infiltrating the sinus mucosa, a few cilia missing, and visible inflammatory cell exudation in the glandular cavity. C) A MRI image showing diffusive mucosal inflammatory cell infiltration and many cilia missing, and a large amount of inflammatory cell exudation in the glandular cavity accompanied with blood cell infiltration.

feasible for operation, so they are often used as an animal model of nasal diseases.[10] In addition, these rabbits have strong survival ability and are able to withstand nasal obstruction with expansion sponges and repeated hypobaric chamber simulations as well as having a strong tolerance to anesthetics. In this study, all procedures, including the obstruction of the nasal cavity with expansion sponges, hypobaric chamber simulation, endoscopic examination, sinus MRI, and sinus mucosal collection required anesthesia treatment. During the whole process, the rabbits were subject to 30-60 min of anesthesia five times each within 12 h. Among the tested 70 rabbits, only 3 died after anesthesia, possibly due to accidental cervical spine injury (all 3 replacement rabbits survived). Overall, the results indicated that white rabbits were suitable for establishing a dynamic SB model, and that intramuscular injection of 5% ketamine combined with Sumianxin II could induce anesthesia with the advantages of rapid onset, good effect, able to be rapidly metabolized, and no obvious accumulation of anesthetics and is suitable for short-term, repeated, rapid anesthetization of rabbits.

To our knowledge, this is the first dynamic SB model in the English as well as Chinese literature. The model has the following advantages: 1) it is simple, less time-consuming, and has no requirement for complex surgical techniques; 2) it does not directly enter the sinus cavity, thus keeping the sinus mucosa sterile and intact; 3) the whole operational process is under a sterile environment (all surgical instruments and sponges are sterile) and could, therefore, avoid the interference of external nasal sinus inflammatory factors; and 4) the expansion of the two expansion sponges inserted in parallel after injection of water and its coupled difference in pressure inside and outside the sinus during ascent/descent could promote the sponges' obstruction of the OMC and prevent inside and outside air exchange, which is the key factor for establishing an SB model. In the study, we conducted hypobaric chamber simulation at four different ascending/descending speeds and two different altitudes to study the dynamic changes of SB and explore the changes of SB animals in behavior, endoscopic morphology, imaging, and cell pathology.

With expansion sponges blocking the OMC of the rabbits, performing hypobaric chamber simulation at an ascending/

Table III. The SB Grade and Maxillary Sinus Mucosal Injures in the Rabbits.

	CILIA MISSING*				INFLAMMATORY CELL INFILTRATION†				GLANDULAR CAVITY INFLAMMATORY CELL EXUDATION‡			
SUBGROUP	−	+	++	+++	−	+	++	++++	−	+	++	+++
1	0	0	1	4	0	0	0	5	0	1	1	3
2	0	0	2	3	0	0	1	4	0	0	3	2
3	0	0	1	4	0	0	0	5	0	0	2	3
4	0	0	2	3	0	0	1	4	0	1	2	2
5	0	3	2	0	0	1	3	1	0	4	1	0
6	0	2	3	0	0	2	3	0	0	3	2	0
7	0	3	1	1	0	3	1	1	0	3	2	0
8	0	4	1	0	0	1	4	0	1	3	1	0
9	1	3	1	0	0	4	1	0	1	3	1	0
10	1	3	1	0	0	5	0	0	1	3	1	0
11	0	4	1	0	1	3	1	0	1	4	0	0
12	1	3	1	0	0	3	2	0	1	4	0	0
13	5	0	0	0	5	0	0	0	5	0	0	0
Control condition	65	0	0	0	65	0	0	0	65	0	0	0
Control group	5	0	0	0	5	0	0	0	5	0	0	0

Based on Kruskal-Wallis rank sum test, *, †, and ‡ indicate $P < 0.05$ for Subgroup 1 vs. Subgroup 5; $P < 0.01$, 0.01, and 0.05 for Subgroup 1 vs. Subgroup 9, respectively; $P < 0.05$ for Subgroup 2 vs. Subgroup 6; $P < 0.05$, 0.01, and 0.05 for Subgroup 2 vs. Subgroup 10, respectively; $P < 0.05$ for Subgroup 3 vs. Subgroup 7; $P < 0.01$, 0.01, and 0.05 for Subgroup 3 vs. Subgroup 11, respectively; $P < 0.05$ for Subgroup 4 vs. Subgroup 8; $P < 0.05$ for Subgroup 4 vs. Subgroup 12; $P < 0.05$, 0.01, and 0.05 for Subgroups 9, 10, and 12 vs. Subgroup 13 and the control group, respectively; $P < 0.01$, 0.05, and 0.05 for Subgroup 11 vs. Subgroup 13 and the control group, respectively; $P < 0.01$ for Subgroups 9, 10, and 11 vs. Subgroup 12 and the control group.

Table IV. Criteria for SB Grading in Rabbits.

	NO. OF TYPICAL BEHAVIOR	ENDOSCOPIC PERFORMANCE	MRI PERFORMANCE	HISTOPATHOLOGICAL LESIONS
Mild	0, 1, or 2	A small amount of watery or mucus-like nasal discharge. Mild turbinate edema; able to perform nasal endoscopy	Sinonasal mucosal edema, exudation and thickening	At least two lesions, up to 1 is moderate
Moderate	2–3	More watery or mucus-like nasal discharge. Turbinate congestion and edema; smaller spacing between the turbinate and nasal septum; unable to perform endoscopy	Nasal mucosal edema, exudation, thickening. High sinus signal, opacification	Three lesions, at least two are moderate
Severe	≥ 4	Large amount of watery or mucus-like nasal discharge, accompanied by blood. Severe congestion and edema of the inferior turbinate; the turbinate is connected with the nasal septum; unable to perform endoscopy	Obvious sinonasal mucosal edema, exudation and thickening, significantly high sinus signal intensity, with a clear indication of fluid level or mucosal avulsion	Three lesions, at least two are severe

Typical behavior included circling, standing, scraping the cage, scratching the face, and breathing with the face up with the histopathological lesions including cilia missing, inflammatory cell infiltration, and glandular cavity inflammatory cell exudation.

descending speed of 15 $m \cdot s^{-1}$ could not induce SB in rabbits, while performing hypobaric chamber simulation at 50 $m \cdot s^{-1}$ to 100 $m \cdot s^{-1}$ will induce SB (Tables II and III and Fig. 1, Fig. 2, and Fig. 3). In addition, without expansion sponges blocking the OMC, performing hypobaric chamber simulation at an ascending/descending speed of 100 $m \cdot s^{-1}$ will not lead to SB. This phenomenon is possibly because the instillation of lidocaine and furacilin mixture in the nasal cavity before endoscopy could lead to OMC peripheral vasoconstriction and subsequently increase sinus ventilation, which makes it less prone to SB (Fig. 1). Based on the rabbits' behavior during hypobaric chamber simulation, changes in endoscopic morphology, MRI, and mucosal pathology, the rapid ascending/descending at speeds of 50 $m \cdot s^{-1}$ to 100 $m \cdot s^{-1}$ and altitudes of 6562 ft or 13,123 ft will lead to SB.

From this animal model, we have shown that the following factors are closely related to the occurrence and severity of SB:

1) The obstruction severity of the OMC. In normal conditions, the sinus mucus glands are confined to areas around the sinus. The OMC is the important common channel of the mucosal ciliature system, with anterior ethmoid, maxillary, and maxillary sinuses to clear nasal sinus secretions. Thus, sinus patency is important to clear nasal secretions.[4,5] OMC obstruction could not only lead to primary SB, but also cause secondary SB from rhinosinusitis.

2) Ascending/descending speeds. When the hypobaric chamber simulated fast ascent to an altitude of 13,123 ft or 6562 ft, the SB severity was significantly greater in the rabbits that ascended at 100 $m \cdot s^{-1}$ than those that ascended at 75 $m \cdot s^{-1}$ and 50 $m \cdot s^{-1}$, but not significantly different between rabbits that ascended at 75 $m \cdot s^{-1}$ and at 50 $m \cdot s^{-1}$. The same is true in the case of fast descent from an altitude of 13,123 ft or 6562 ft to sea level. The results showed the greater the ascending/descending speed, at the same descending/ascending altitude (0 ft-13,123 ft), the greater the SB severity in rabbits with OMC obstruction.

3) Flight altitude. The results indicated that when at rapid ascending/descending speeds, SB was mainly induced during the flight altitude between 0 ft and 6562 ft. This was primarily caused by the difference in air pressure at altitude. It is well known that air pressure drops in a nearly exponential manner with increasing altitude. The changes in air pressure are more dramatic at altitudes closer to sea level and less dramatic at higher altitudes. For example, the change in air pressure is 11.5 kPa (86 mmHg) at altitude in the range of 0 ft–3281 ft, 10.4 kPa (78 mmHg) at altitude in the range of 3281 ft–6562 ft, and 9.4 kPa (70 mmHg) at altitude in the range of 6562 ft–9842 ft. This is because the impact of Earth's gravity on the atmosphere is far greater than the warming effect of solar radiation. Thus, most of the air is concentrated on the Earth's surface. The closer to the ground the air is, the higher the atmospheric density, and vice versa. In this study, the magnitude of change in air pressure was 21.9 kPa (164 mmHg) when ascending/descending from 0 ft–6562 ft and 17.9 kPa (134 mmHg) when ascending/descending from 6562 ft–13,123 ft. The pressure difference between the two was 4.0 kPa (30 mmHg), which is consistent with the conclusion of the study that at the same ascending/descending speeds, SB occurs mainly at altitudes lower than 6562 ft.

Thus, it could be concluded that pilots with acute rhinitis should be forbidden to fly. Active treatment should be applied to pilots with chronic rhinitis, including sinusitis, nasal polyps, allergic rhinitis, and sinus cysts, all of which would obstruct the OMC. Cabin environments should be improved, cabin impermeability should be enhanced, and pressurization facility should be perfected.[22,25] A plane's ascending/descending speed should be appropriate. When pilots feel pain in their sinuses when descending, they could ascend to the original height before descending slowly to balance the internal and external pressure of the sinuses, if permitted.[16,23]

Sinus barotrauma is a dynamic process closely related to flight speed and altitude. Most studies on SB are limited to static status with the same altitude and speed. In this paper, we established a dynamic SB model with different ascending/descending speeds and flight altitudes with the hope of providing a reference

for further studies on dynamic SB pathogenesis and control measures.

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