Progress in Immunology 2023; 3(1): 58.
Original Research Article

Establishment and evaluation of a rat model of inhalation lung injury induced by ship smoke

Xinxin Duan[1], Jin Dong[2], Shang He[3], Chengbin Wang[2], Haiwei Zhou[1,*]

[1] *Division I of Diagnositic for Infectious Diseases, Institute for In Vitro Diagnostics Control, National Institutes for Food and Drug Control, Beijing 100050, China*

[2] *Department of Clinical Laboratory, General Hospital of PLA, Beijing 100853, China*

[3] *Shanghai WuXi Diagnostics Technology Co.,Ltd., Shanghai 200131, China*

*** Corresponding author:** Haiwei Zhou, zhouhaiwei@nifdc.org.cn

ARTICLE INFO

Received: 4 May 2023
Accepted: 14 July 2023
Available online: 21 August 2023

http://dx.doi.org/10.59400/fls.v5i2.1626

ABSTRACT: Objective: We aimed to establish and evaluate a rat model of inhalation lung injury induced by ship smoke. **Methods:** We monitored the changes of oxygen, carbon monoxide, carbon dioxide and hydrogen sulfide concentration within 20 min after combustion of ship materials with a AIKE four in one gas detector. We detected the changes of arterial blood gas, coagulation time, and lung moisture content (%). Macroscopic and microscopic changes in lung tissue were observed to understand the degree of lung injury. **Results:** We set 5 g ship materials and smoked 15 min as experimental conditions. Metabolic acidosis in the early stage after inhalation, but metabolic acidosis combined with respiratory acidosis in later stage. Histopathological observation showed diffuse hemorrhage, edema and inflammatory cell infiltration in lung tissue as manifestations of lung injury, and the injury did not recover at 72 h after inhalation, the change of blood coagulation function was not statistically significant. **Conclusion:** A rat model of inhalation lung injury induced by ship smoke was successfully established, which has the advantages of easy replication, stability and reliability. It can be used to research and treatment inhalation lung injury induced by ship smoke in naval war environment and other cases.

KEYWORDS: ship smoke; inhalation injury; models; animal

1. Introduction

With the development of science and technology, various types of large-scale, automatic, high-speed ships are more and more used in coastal defense[1]. Fire load composition is more and more complex, resulting in various types of ship fire, explosion accidents frequently occur[2,3]. The internal non-metallic materials in the ship release a large amount of toxic gas, dust and particulate matter, the crew is very susceptible to inhalation of toxic gases caused by acute respiratory and lung injury[4], and even developed into respiratory failure. In recent years, the application of a large number of new composite materials on naval ships has increased the complexity of the smoke components, mainly including harmful gases such as carbon monoxide (CO), carbon dioxide (CO_2), hydrogen sulfide (H_2S) and nitrogen oxidex (NOx), and sometimes even contains highly toxic gases such as hydrogen chloride, cyanide and hydrogen cyanide[5]. The harm to the human body is much greater than the toxicity of a single toxic gas. In severe cases, death can occur quickly[6]. The fire and explosion accidents of warship have become one of the hot topics at home and abroad[7]. Smoke inhalation is the leading cause of

acute lung injury (ALI), acute respiratory distress syndrome (ARDS), or even serious respiratory failure in military personnel[8]. It is generally believed that inflammatory cells and release of inflammatory mediators, especially neutrophils and macrophages, are mandatory in the pathological process of smoke inhalation-induced acute lung injury[9,10]. However, the role of adaptive immune cells in this disease is less well defined. For smoke inhalation studies, in vitro models are limited in their ability to capture all aspects of smoke inhalation injury pathophysiology and the complex clinical features of human smoke inhalation injury. For these reasons, animal models of smoke inhalation injury are needed to uncover the post-smoke inhalation injury pathological mechanisms and test novel therapeutic approaches[11]. In order to further explore the pathogenesis, drug prevention and therapeutic effect evaluation of lung damage caused by naval ship smoke, it is necessary to construct a stable and reliable animal model. On the basis of the analysis platform of lung injury induced by gunpowder smoke constructed in the early stage of the study group, the smoke device of inhaled lung injury induced by smoke in rats was made[8]. In this study we established a rat model of inhalation lung injury induced by smoke inhalation, and evaluated it.

2. Materials and methods

2.1. Experimental animals

Clean, healthy, adult male Wistar rats, weight 150 g–200 g, were provided by the experimental animal center of the General Hospital of the People's Liberation Army[SCXK-(JING)-2016-2006].

The rats were fed in single cage with temperature 22 ℃–24 ℃, humidity 50%–60%, 12 h rhythm day and night, eating and drinking freely. The animals were treated according to the guidelines of the experimental animal ordinance. This study was carried out in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animal of the National Institutes of Health. The animal use protocol has been reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of the General Hospital of the People's Liberation Army.

2.2. Instrument and equipment

2.2.1. Smoke generator

As shown in **Figure 1** below (A is the front view, B is the vertical view), the self-made smoke inhalation injury device consists of two parts: a smoke chamber (the right) and an animal chamber (the left). A hole in the middle of the two chambers is connected, and a fan is arranged inside the smoke chamber to allow the smoke to circulate evenly throughout the device. Smoke indoor diameter 31 cm × 40 cm × 28 cm, built-in remote electromagnetic heater, smoke iron plate, drum fan. Animal indoor diameter to 31 cm × 40 cm × 28 cm, the perspective window of the room wall is used to observe the smoke of the animal after the situation, the external wall of smoke detector monitoring device inside the composition of the ship smoke, including O_2, CO, CO_2, H_2S, and remote induction cooker switch, temperature and humidity monitor for real-time monitoring of the temperature and humidity in the smoke device, the entire experimental process temperature remained around 37 ℃.

Figure 1. Smoke generator.

2.3. Smoke material

Seven kinds of ship non-metallic materials (Gifts from the Department of Respiratory Medicine, Naval General Hospital).

Poly double horse (Ill type) foam material: main component Bismaleimide polymer; NH/Fullers Foamed Rubber and Plastic Insulation Products: Main Components Rubber and Plastic Compounds; EA-100 Flame Retardant White rubber: The main components of adhesives, inorganic fillers; LZN-1 high-performance Damping Material: main components of rubber, vulcanizing agent, adhesives, etc.; JYJPJ85/SC Marine Low Smoke halogen free cable: The main group is divided into polyethylene propylene plastic; WQF-2 Silicone Propylene Latex Paint: Main Components Silicone Propylene Latex; Rhyme decorative board: the main components of aluminum, wood, adhesive.

Seven Kinds of non-metallic materials of ships, weighing and then cut into uniform small pieces, and sealed in a clean plastic bag for storage.

2.4. Experiment design

2.4.1. Relationship between ship material quantity, exposure time and mortality in rats

(1) Rats（n = 6） were exposed at different times (8 min, 10 min, 15 min, 18 min, 20 min) with a fixed amount of ship material (5 g); (2) The rats (n = 6) were exposed to different ships material quantities (3 g, 5 g, 8 g, 10 g) under the condition of fixed fumigation time (20 min) respectively. Record and analyze the whole process of smoking and the survival status of rats in 72 h after fumigation treatment.

2.4.2. Animal grouping and injury

42 Wistar rats were randomly divided into control group and 2 h, 6 h, 12 h, 24 h, 48 h, 72 h group (n = 6) after injury. The rats in the injury group were placed in closed smoke box and exposed to 15 min in smoke produced by 5 g ship materials. After the end of the injury, the animals were put back to the cage and killed respectively. In the control group, rats were exposed to 15 min in the air of the smoke box, and were executed after exposure to 72 h.

2.4.3. Methods of injury

The ship materials with the proportion weighing and processing were put on the iron plate of the smoke chamber, placed on the remote induction cooker heater, and closes the door of the smoke chamber. Opening the door of the animal room and close it after putting in the rat to be injured.

Checking the air tightness of the unit and turn on the main power switch of the fume generator, the gas composition analyzer, the gas sampling pump and the temperature and humidity monitor switch. Using a remote control device, turn on the switch of the heater of the induction cooker and adjust it to the maximum power bracket. After 1 min, the smoke room can be observed to be filled with smoke rapidly, and after heating 5 min, the electromagnetic heater can be turned off. After exposure time is reached, open the animal room and remove the rats and place them in the air.

2.5. Detection index

2.5.1. Concentration and temperature of O_2, CO, CO_2, H_2S in smoke

The concentration of each gas component and the temperature of smoke were measured at 5 min, 10 min and 18 min after combustion of ship materials.

2.5.2. Clinical manifestation

The state of mind, activity, breathing and cyanosis of the rats after inhaling the smoke and after the injury were observed. The rats developed restlessness, shortness of breath, large mouth breathing, wheezing, and gradually appearing cherry red to purple in the skin of mouth and nose.

2.5.3. Arterial blood gas

The rats were intraperitoneally injected with 10% chloral hydrate (0.35 ml/100 g) at the corresponding time points. The abdominal aorta was separated from the abdominal aorta, and the rats were killed after taking the blood for 1 ml. The arterial blood gas analysis was performed within half an hour.

2.5.4. Coagulation function

The blood of the abdominal aorta was placed in the anticoagulant coagulant tube of sodium citrate, and the coagulation function was to be measured.

2.5.5. The lung water content of tissue

After taking the right anterior lobe of the lung, the filter paper swabs the dry surface of the blood, weighed (wet weight) on the electronic balance, and then baked the oven for 48 h to constant weight at 70 ℃, and weighted (dry weight) in the electronic balance, and calculated the water content of the lung (%).

2.5.6. Pathological examination of the lung tissue

After the opening of the chest, the general changes of the lung were observed. The lower lobe of the right lung was immersed in 10% neutral formaldehyde solution and fixed in paraffin. After hematoxylin-eosin staining, light microscopy was used for observation.

2.6. Statistical analysis

SPSS version 17.0 software was used for the data analysis, and the experimental results were compared. The data are presented as the mean ± standard deviation; the comparison used was a single-factor analysis of variance (one-way ANOVA) between multiple groups, comparisons between each group were performed using an LSD test, and $P < 0.05$ was considered statistically significant. The survival data of each group were compared by survival analysis.

3. Results

3.1. Relationship between ship materials quantity, exposure time of rats and mortality rate

The fixed ship material is 5 g, the exposure time is 8 min, 10 min, 15 min, 18 min, 20 min. When the fixed exposure time is 20 min, and the ship materials were 3 g, 5 g, 8 g, and 10 g respectively, the survival curves of rats after smoking treatment were shown in **Figure 2** below.

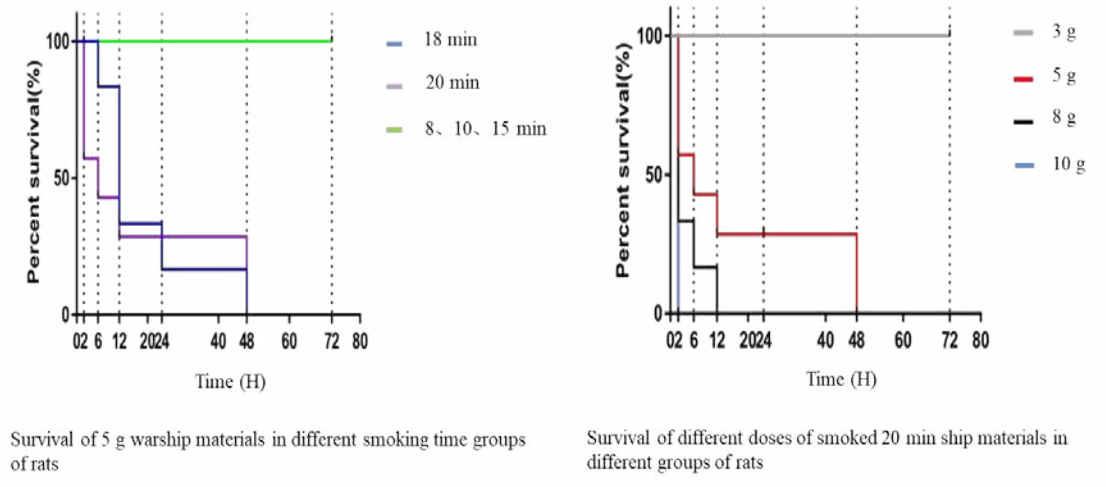

Figure 2. The survival situation of each group of rats after fixing the material quantity and smoking time of the ship respectively.

3.2. Determination of concentrations of O_2, CO, CO_2 and H_2S in smoke

There is no significant difference between the concentrations of O_2, CO, CO_2, H_2S and temperature in the 5 min, 10 min, 15 min, 18 min, and cigarette cases of the 5 min, 10 min, 15 min, and 18 min ($P < 0.05$, for example, **Table 1**)

Table 1. Variation of gas concentration and temperature at different time points after ship smoke formation (X ± S, n = 6).

Time (min)	O_2 (%)	CO (ppm)	CO_2 (%)	H_2S (ppm)	T (℃)
5	18.48 ± 0.23	843.88 ± 16.15	8.61 ± 0.44	82.14 ± 1.59	27.01 ± 0.62
10	18.28 ± 0.29	842.38 ± 12.61	8.19 ± 1.02	82.62 ± 2.64	26.95 ± 0.55
15	18.21 ± 0.35	838.75 ± 12.09	7.99 ± 0.48	82.25 ± 1.48	26.84 ± 0.61
18	18.20 ± 0.32	831.63 ± 8.57	8.00 ± 0.46	82.36 ± 1.88	26.65 ± 0.91
F Value	1.423	1.492	1.618	0.092	0.430
P Value	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$	$P > 0.05$

ppm: parts per million
CO 1 ppm = 2.86×10^{-8} mol/L; H_2S 1 ppm = 1.94×10^{-8} mol/L

3.3. Clinical manifestations

At the end of the experiment, the rats in the control group had no abnormality, but good mental state, normal activity, sensitive response, smooth breathing and smooth coat, while the rats in the injury group had shortness of the breath during the smoking process, open mouth breathing. After the experiment, the rats could be observed to have more mouth and nose secretions, moist gloss hair, and wheezing sounds, and cyanosis in limbs and lips.

3.4. Results of arterial blood gas analysis

Hypoxemia occurs in the early stages of smoke inhalation injury, with partial pressure of oxygen (PaO_2) reaching a minimum 2 h after smoke inhalation before gradually recovering. The partial pressure of carbon dioxide ($PaCO_2$) began to rise gradually after inhalation of smoke, 6 h peaked, and decreased recovery gradually. The carbon-oxygen hemoglobin (COHb) peaked 2 h after smoke inhalation and then gradually recovered. The oxyhemoglobin (O_2Hb) begins to decrease after smoke inhalation, decreases to a minimum of 2 h and gradually recovers. The oxygen saturation (SO_2) gradually decreases after smoke inhalation, reaches a minimum of 2 h, and then gradually returns to normal, as shown in **Table 2**.

Table 2. The changes of arterial blood gas and lung water content (X ± S, n = 6).

Grouping	Number	PH	PO_2 (mmHg)	PCO_2 (mmHg)	SO_2 (%)	O_2Hb (%)	COHb (%)	Moisture content of lung (%)
Control group	6	7.42 ± 0.040	84.22 ± 0.701	41.64 ± 1.621	89.86 ± 5.429	87.96 ± 7.150	0.6 ± 0.212	0.74 ± 0.002
2 H	6	7.24 ± 0.049**	52.0 ± 1.512**	45.6 ± 2.132*	76.3 ± 7.131*	81.64 ± 2.439	7.36 ± 1.099**	0.80 ± 0.013*
6 H	6	7.28 ± 0.043**	64.42 ± 1.46**	54.16 ± 5.183**	86.68 ± 7.235	87.48 ± 5.643	2.06 ± 0.882	0.82 ± 0.025*
12 H	6	7.37 ± 0.055	70.44 ± 1.396**	42.52 ± 3.618	87.38 ± 10.021	90.9 ± 7.536	1.48 ± 1.228	0.79 ± 0.016*
24 H	6	7.45 ± 0.010	82.78 ± 1.094	41.92 ± 2.141	88.68 ± 8.089	92.9 ± 2.473	1.02 ± 1.057	0.76 ± 0.014*
48 H	6	7.46 ± 0.027	83.3 ± 1.251	40.68 ± 1.668	91.36 ± 8.01	93.66 ± 4.005	1.26 ± 1.592	0.75 ± 0.004
72 H	6	7.44 ± 0.035	83.76 ± 1.238	40.86 ± 1.330	86.2 ± 10.479	92.26 ± 5.456	1.2 ± 1.478	0.75 ± 0.006
F Value *P* Value		24.404 $P < 0.001$	497.191 $P < 0.001$	14.381 $P < 0.001$	1.784 $P > 0.05$	3.148 $P < 0.05$	20.522 $P < 0.001$	28.549 $P < 0.001$

PS: * compared with control group, $P < 0.05$; ** compared with control group, $P < 0.01$

3.5. Results of coagulation function in each group

The analysis of the results of coagulation function in each group after inhalation of smoke in rats, the PT decreased in the 2 h group compared with the control group, with statistically significant ($P < 0.05$), the 48 h group compared with the control group, TT decreased, statistically significant ($P < 0.01$), and the 72 h group compared with the control, the fibrin degradation product (FDP) decreased, statistically significant ($P < 0.05$), While the APTT, FIB, D-dimer (D-D), antithrombin (AT) were not statistically significant compared with the control group, so it is suggested that the smoke inhalation injury of the ship in this model may not cause the massive coagulation dysfunction, as shown in **Table 3** below.

Table 3. The changes in coagulation function (X ± S, n = 6).

Grouping	PT	APTT	TT	FIB	DD	AT3	FDP
Control group	20.83 ± 0.94	26.13 ± 3.88	34.87 ± 1.81	2.63 ± 0.55	0.17 ± 0.03	117.5 ± 7.29	1.97 ± 0.25
2 H	19.30 ± 1.29*	23.42 ± 1.43	33.82 ± 3.70	2.81 ± 0.28	0.18 ± 0.06	113.0 ± 12.69	1.80 ± 0.45
6 H	19.80 ± 1.08	24.28 ± 3.57	43.32 ± 15.07	2.96 ± 0.25	0.19 ± 0.09	111.2 ± 9.75	1.71 ± 0.57
12 H	20.13 ± 0.85	23.38 ± 2.51	39.47 ± 8.38	3.00 ± 0.62	0.20 ± 0.09	112.7 ± 13.91	1.77 ± 0.65
24 H	19.87 ± 0.83	23.73 ± 2.19	44.17 ± 12.91	2.55 ± 0.54	0.19 ± 0.06	110.7 ± 6.12	1.79 ± 0.69
48 H	20.45 ± 1.21	27.77 ± 4.95	56.68 ± 8.56**	2.75 ± 0.19	0.17 ± 0.09	116.2 ± 8.99	1.77 ± 0.66
72 H	20.21 ± 1.03	22.75 ± 2.31	36.82 ± 7.79	2.62 ± 0.40	0.18 ± 0.04	120.3 ± 8.04	1.07 ± 0.58*
F Value *P* Value	1.332 $P > 0.05$	1.925 $P > 0.05$	4.209 $P < 0.05$	0.944 $P > 0.05$	0.115 $P > 0.05$	0.663 $P > 0.05$	1.504 $P > 0.05$

PS: * compared with control group, $P < 0.05$; ** compared with control group, $P < 0.01$

3.6. The pathological changes of the lung tissue

The lung in general view showed that the rats in the injured group had obvious hyperemia and edema in smoke inhalation within 24 h, and there were needle-like inhalation bleeding spots on the surface of the lung in early stage. There were many spots of patchy bleeding, white foamed liquid in the trachea and bleeding spots in the 72 h lungs. In control group, the lungs were fleshy pink, the color was uniform, and there was no swelling, bleeding and necrosis (see below **Figure 3**).

Under light microscope, it was observed that the rats in the injury group suffered hemorrhage and edema after inhaling smoke for 2 h, the infiltration of erythrocytes and inflammatory cells in the alveolar cavity was observed for 6 h, the infiltration of erythrocytes and inflammatory cells was observed for 12 h, the alveolar cavity was widened, the septum thickened, and 72 h erythrocytes and inflammatory cells decreased (see **Figure 4** below).

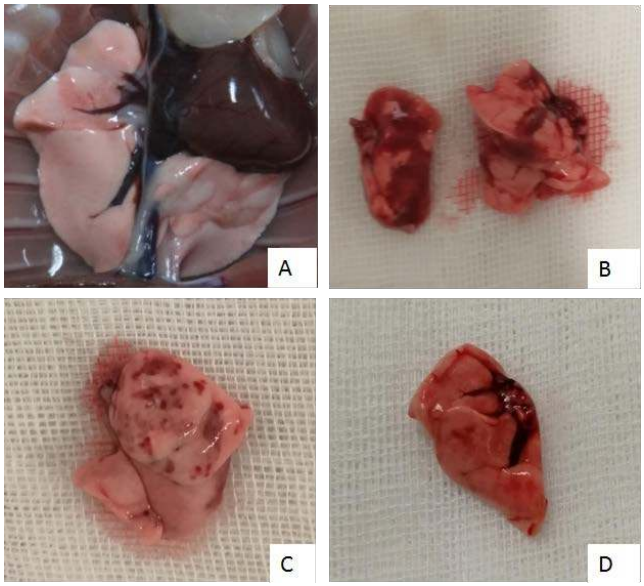

Figure 3. General view of lung tissue. **A:** Control group; **B:** 2 h group; **C:** 12 h group; **D:** 72 h group.

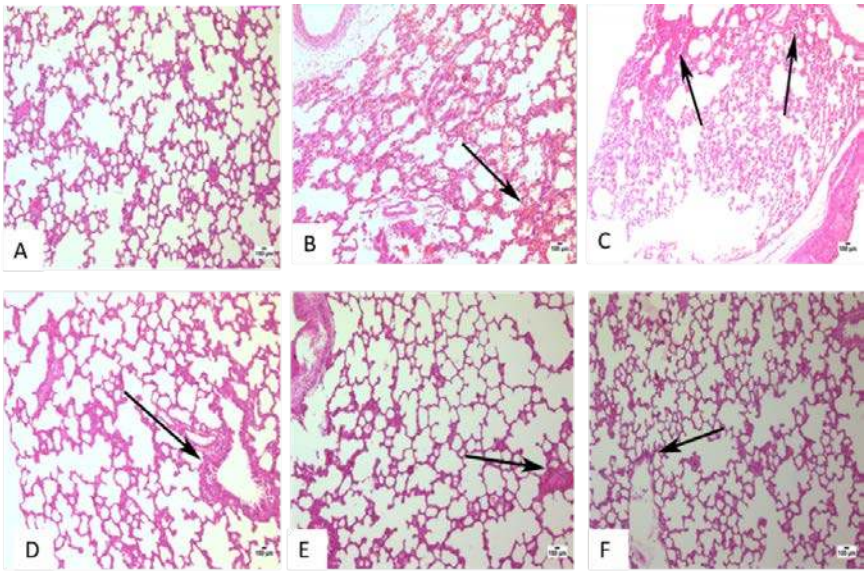

Figure 4. Pulmonary histopathology changes. **A:** Control group; **B:** 2 h group; **C:** 6 h group; **D:** 12 h group; **E:** 24 h group; **F:** 72 h group. Representative images of hematoxylin and eosin-stained lung sections showed obvious thickening of the alveolar wall, interstitial edema and infiltration of inflammatory cells in rats with smoke inhalation. Scalebars, 100 μm.

4. Discussion

Smoke inhalation is common in fire, war and other environment, mainly by the size of suspended particles and toxic gas composition, the composition is more complex, as many as 250 kinds[12]. In the past, the smoke materials used in the inhalation lung injury model were mainly dried pine chips and kerosene, and the rats were inhaled in the apparatus after anesthesia, and the respiration and other physiological activities in the rats were weakened, which would have a great effect on the result of the model[13,14]. In our study, a self-made smoke inhalation injury device was used to inhale and eliminate anesthesia and other effects in the normal active state of rats. 7 kinds of non-metallic materials from the Department of Respiration of Naval General Hospital were used to simulate the environment of ship combustion, to construct the model of the lung injury induced by ship smoke, and to lay a foundation for further study on the lung injury caused by ship smoke.

The smoke inhalation injury device is divided into a smoke room and an animal room, which are independent of each other and exclude other injury factors that may result from the burning of ship materials, so as to ensure that smoke inhalation is a single injury factor. Smoke produced in the smoke room circulates evenly under the action of fan airflow throughout the device. Built-in remote-controlled electromagnetic heater to avoid opening the cabin perspective door leads to inconsistent combustion conditions each time, the external smoke and temperature and humidity detector real-time monitoring to ensure the consistency of building model conditions, reliability and stability. In addition, the self-made device is small in size, simple in manufacture and easy to be popularized and applied.

In this study, by changing the burning quantity of the ship materials and exposure time and observing the survival of rats within 72 h, it was found that the death rate of rats increased with the increase of ship material quantity and exposure time, and when the exposure time was 20 min, half of the lethal amount of the rats was between 5 g and 8 g. The ship material quantity was 5 g and the exposure time was 18 min, the death rate of ship materials was 83.3% within 24 h. The exposure time was reduced to 15 min and no rat died within 72 h. Finally, 5 g ship material and 15 min exposure were selected as the injury conditions. Combustion of seven types of non-metallic materials on ships consists mainly of harmful gases such as CO, CO_2, H_2S and NOx, and sometimes even contains highly toxic gases such as hydrogen chloride, cyanide and hydrogen cyanide[15]. In this study, the concentration of CO, CO_2, H_2S, the temperature and humidity in the fume generator remained stable within 15 min of smoke production. CO is caused by incomplete combustion of carbon-containing compounds. It is produced in large quantities in all fires and is harmful to humans and can cause neurotoxicity and vascular toxicity[16]. It is also a toxic gas that has been proven to cause death, with carbon compounds completely burning to form CO_2[17], and studies have shown that CO_2 is also one of the factors that cause lung damage[18]. Based on the relationship between inhalation of different concentrations of CO and poisoning degree[19], the smoke inhalation damage model was made by continuous inhalation of smoke in airtight condition.

Hypoxemia occurs in the early stages of smoke inhalation lung injury in ships, research shows that oxygen partial pressure (partial pressure of oxygen, PaO_2) in smoke inhalation after 2 h to the lowest value, and gradually recovered. The partial pressure of carbon dioxide ($PaCO_2$) begins to rise after smoke inhalation, peaking at 6 h. Carbon-oxygen hemoglobin (COHb) is produced by combining hemoglobin with CO after inhalation. It is 250 times higher than the ability to bind to oxygen[20], making hemoglobin lose its ability to transmit oxygen, leading to lung hypoxia and injury, so it can be considered as an indicator of CO poisoning[21]. The COHb levels begin to rise after smoke inhalation,

peak at 2 h and then begin to decline gradually. The pulmonary water content is a good index for evaluating pulmonary edema and can also indicate pulmonary microvascular permeability. The increase of pulmonary water content in this model suggested that the pulmonary microvascular permeability of rats increased. Smoke inhalation directly affects the airways, causing endothelial damage and increased hydrostatic pressure in blood vessels, which in turn produces pulmonary edema, affects pulmonary ventilation, further aggravates tissue hypoxia, activates the lung defense system, stimulates the release of a large number of inflammatory factors, and leads to a vicious circle. The histopathological observation showed that the rats in the injury group suffered hemorrhage and edema after 2 h inhalation of smoke, 6 h showed leakage of erythrocyte and inflammatory cells infiltration in the alveolar cavity, 12 h in addition to erythrocyte and inflammatory cells infiltration, while the alveolar cavity widened, thickened septum, 72 h erythrocyte and inflammatory cells decreased.

In conclusion, the rat model of inhaled lung injury was successfully established by exposing 15 min to smoke from 5 g warship material using the self-made smoke emitting device of the research group. The model can cause pulmonary hemorrhage, edema, inflammatory infiltration of the airway, achieving the expected injury. It was stable and easy to replicate, and did not cause asphyxia and death in rats. This model can be adjusted according to different experimental requirements, used for cytological experiments, modified ship materials and proportions, etc. It is suitable for the research of early pathogenesis and experimental treatment of smoke inhalation injury in ships.

Author contributions

Conceptualization, CW; methodology, XD and JD; validation, SH; formal analysis, XD and JD; investigation, XD and JD; resources, SH; data curation, XD and JD; writing—original draft preparation, XD and JD; writing—review and editing, XD and JD; visualization, XD and JD; supervision, HZ; project administration, HZ; funding acquisition, CW. All authors have read and agreed to the published version of the manuscript.

Acknowledgments

This work was funded by the Research Project of the Whole Army Logistics Research Project (BHJ16J011).

Conflict of interest

The authors declared no conflict of interest.

Research data availability statement

All data used in this manuscript have been reported. The authors will freely share any further information upon request.

References

1. Shen J, Ma X, Qiao W. A model to evaluate the effectiveness of the maritime shipping risk mitigation system by entropy-based capability degradation analysis. *International Journal of Environmental Research and Public Health* 2022; 19(15): 9338. doi: 10.3390/ijerph19159338
2. Wu H, Hu Y, Wang W, et al. Ship fire detection based on an improved YOLO algorithm with a lightweight convolutional neural network model. *Sensors* 2022; 22(19): 7420. doi: 10.3390/s22197420
3. Puisa R, Williams S, Vassalos D. Towards an explanation of why onboard fires happen: The case of an engine room fire on the cruise ship "Le Boreal". *Applied Ocean Research* 2019; 88: 223–232. doi: 10.1016/j.apor.2019.04.020

4. Lee AS, Mellins RB. Lung injury from smoke inhalation. *Paediatric Respiratory Reviews* 2006; 7(2): 123–128. doi: 10.1016/j.prrv.2006.03.003
5. Fonollosa J, Solórzano A, Marco S. Chemical sensor systems and associated algorithms for fire detection: A review. *Sensors* 2018; 18(2): 553. doi: 10.3390/s18020553
6. Xu LJ, Chen Q, Xiao CJ, et al. Qualitative analysis of the smoke composition of nonmetal materials of ships in combustion. *Journal of Navy Medicine* 2005; 26(1): 8–11. doi: 10.3969/j.issn.1009-0754.2005.01.004
7. Luo JH, Jiang YS, Chen LN. Characteristic and prevention as well as control of harmful gases causing by fire disaster in naval vessels chambers. *Journal of Navy Medicine* 2009; 30(2): 105–107. doi: 10.3969/j.issn.1009-0754.2009.02.004
8. Zhang F, Li M, Lan Y, Wang C. Imbalance of Th17/Tregs in rats with smoke inhalation-induced acute lung injury. *Scientific Reports* 2016; 6: 21348. doi: 10.1038/srep21348
9. Williams AE, Chambers RC. The mercurial nature of neutrophils: Still an enigma in ARDS? *American Journal of Physiology—Lung Cellular and Molecular Physiology* 2014; 306: L217–L230. doi: 10.1152/ajplung.00311.2013
10. Aggarwal NR, King LS, D'Alessio FR. Diverse macrophage populations mediate acute lung inflammation and resolution. *American Journal of Physiology—Lung Cellular and Molecular Physiology* 2014; 306: L709–L725. doi: 10.1152/ajplung.00341.2013
11. Abdullahi A, Amini-Nik S, Jeschke MG. Animal models in burn research. *Cellular and Molecular Life Sciences* 2014; 71(17): 3241–3255. doi: 10.1007/s00018-014-1612-5
12. Ballardcroft C, Sumpter LR, Broaddus R, et al. Ovine smoke/burn ARDS model: A new ventilator-controlled smoke delivery system. *The Journal of Surgical Research* 2010; 164(1): e155–e162. doi: 10.1016/j.jss.2010.05.042
13. Leiphrakpam PD, Weber HR, McCain A, et al. A novel large animal model of smoke inhalation-induced acute respiratory distress syndrome. *Respiratory Research* 2021; 22(1): 198. doi: 10.1186/s12931-021-01788-8
14. Mercel AI, Gillis DC, Sun K, et al. A comparative study of a preclinical survival model of smoke inhalation injury in mice and rats. *American Journal of Physiology—Lung Cellular and Molecular Physiology* 2020; 319(3): L471–L480. doi: 10.1152/ajplung.00241.2020
15. Xu LJ, Xiao CJ, Chen Q, et al. Quantitative analysis of the smoke composition formed by the burning of 7 nonmetal materials within the naval ship. *Chinese Journal of Nautical Medicine and Hyperbaric Medicine* 2009; 16(2): 117–119. doi: 10.3760/cma.j.issn.1009-6906.2009.02.025.
16. Dries DJ, Endorf FW. Inhalation injury: Epidemiology, pathology, treatment strategies. *Scandinavian Journal of Trauma Resuscitation & Emergency Medicine* 2013; 21(1): 1–15. doi: 10.1186/1757-7241-21-31
17. Zhao J, Zhu MX, Lu YM. Toxic gases in fire smoke and mechanism of poisoning. *Chinese Journal of Emergency Medicine* 2004; 13(7): 497–498. doi: 10.3760/j.issn:1671-0282.2004.07.031.
18. Abolhassani M, Guais A, Chaumet-Riffaud P, et al. Carbon dioxide inhalation causes pulmonary inflammation. *American Journal of Physiology, Lung Cellular & Molecular Physiology* 2009; 296(4): L657–L665. doi: 10.1152/ajplung.90460.2008
19. Li JX, Xia T, Qin WH, et al. The correlation analysis of indoor carbon monoxide concentration and chronic diseases. *International Journal of Laboratory Medicine* 2015; (16): 2326–2328. doi: 10.3969/j.issn.1673-4130.2015.16.015.
20. Gozubuyuk AA, Dag H, Kacar A, et al. Epidemiology, pathophysiology, clinical evaluation, and treatment of carbon monoxide poisoning in child, infant, and fetus. *Northern Clinics of Istanbul* 2017; 4(1): 100–107. doi: 10.14744/nci.2017.49368
21. Lange M, Cox RA, Enkhbaatar P, et al. Predictive role of arterial carboxyhemoglobin concentrations in ovine burn and smoke inhalation-induced lung injury. *Experimental Lung Research* 2011; 37(4): 239–245. doi: 10.3109/01902148.2010.538133