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Propofol Regulates the Expression of BecliN-1 through miR-30b and Protects against Lung Ischemia-Reperfusion Injury

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ABSTRACT

Pulmonary ischemia-reperfusion can cause severe dysfunction of alveolar epithelium and alveolar cells. Drugs such as propofol have a protective effect on lung ischemia-reperfusion, but this protective mechanism is not stable and requires other factors such as nucleosides. The purpose of this article is to study the protective mechanism of propofol on lung ischemia-reperfusion injury by regulating the expression of BecliN-1 by miR-30b. With 72 male rats as the research object, a rat lung ischemia-reperfusion model was established. Phenol agents were perfused as the perfusion solution to detect the expression levels of miR-30b and BecliN-1, statistical experimental data and analyze the regulatory mechanism of miR-30b on the expression of BecliN-1 and the effect of propofol on the protection of lung ischemia-reperfusion. Research results show that propofol can reduce inflammation, reduce oxidative stress, inhibit lung tissue apoptosis, improve lung function and pathological changes of lung tissue by inhibiting the activation of the JAK-STAT signaling pathway, and propofol can pass. The protection of miR-30b's regulation of BecliN-1 expression against lung ischemia-reperfusion injury is 30% higher than that of other protective mechanisms. At the same time, the apoptosis rate of inflammatory lung tissue cells is reduced by 13%.

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Introduction

Propofol is a new type of intravenous anesthetic. It is completely reliable and is widely used in sedative clinical anesthesia and intensive care medicine (1). With the deepening of its research, the understanding of its role has gradually deepened. Isopropanol is very similar in chemical structure to endogenous antioxidants, known as butyraldehyde solvent with antioxidant effect (2). Therefore, isopropanol also has an antioxidant effect. Its role is to reduce tissue oxygen consumption, directly scavenge free radicals, inhibit lipid peroxidation and regulate cellular calcium balance. The antioxidant effect of propofol is similar to ivy or BHT. It directly reacts with free radicals to form 2,6-diisopropylphenoxy and deactivates the free radicals (3).

Studies have shown that propofol not only has anesthetic effects but also has many other biological effects, such as lung protection. Studies have shown the effect of propofol on the central nervous system is similar to that of barbiturates (4). It can cause pulmonary vasoconstriction, decreased pulmonary blood flow, decreased intracranial pressure and decreased lung oxygen metabolism. However, recent studies have found that the level of lung protection provided by various anesthetics is disproportionate to the decline in lung metabolism caused by them. Most animal studies and clinical studies have confirmed that propofol has certain protection against lung ischemia and hypoxia injury. It is a very promising neuroprotective drug during the perioperative period (5). However, the mechanism of its neuroprotection has not been fully elucidated, so it is necessary to study the mechanism of neuroprotection.

The protective effect of propofol on lung ischemia-reperfusion injury is related to calcium antagonism, free radical ablation, inhibitory amino acids and neuronal metabolism. More and more studies have confirmed that propofol has antioxidant properties related to phenolic genes role (6). It can react with free radicals in the chemical structure, similar to the endogenous antioxidant vitamin E (7). It is speculated that propofol can restore ATPase activity by improving antioxidant capacity and plundering

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excessive free radicals. Since the reabsorption of amino acids by contraction of ischemic tissue is a process of ATP consumption, anesthetics including propofol can reduce tissue energy consumption and increase moderate memory, thereby playing a protective role in the large lungs. At the same time, propofol has calcium channel blockade (8). This effect can reduce the moderate rate of decrease and Ca influx in the ischemic phase, thereby helping to restore ATP during reperfusion and reducing the damage to lung ischemia and hypoxia (9). However, the concentration of MDA under propofol anesthesia did not increase after ischemia-reperfusion injury, indicating that propofol plays a protective role in the lungs through an antioxidant mechanism (6).

The miR-30b is a type of endogenous small RNA with a length of about 22 nucleotides and plays an important role in gene transcription. In the human genome, there are almost 1000 miR-30b, and each miR-30b can have hundreds of marc targets (10). All miR-30bs in cells regulate at least 30% of the gene expression of all genetic material, so they can be the main participants in the activity control center and participate in almost all cellular functions, such as growth, differentiation, and disease cell (11, 12).

A large number of miR-30b with different functions can regulate the expression level of human genes. MiR-30b is synthesized by a variety of tissues and cells and is widely distributed in human organs and tissues. These organs play important biological functions in cell proliferation, differentiation and functional maintenance (12). There is no doubt that the expression of miR-30b is also an important regulatory factor for its development (13). Lung cancer is not yet fully understood, and the genes, genome, and the mechanism of CRC metastasis are not fully understood, especially the key mechanism of CRC metastasis and its signal transduction pathways are precisely controlled. miR-30b-30a is miR-30b-30 Members of the family (14). In the current study, we evaluated the effect of propofol on the expression of BecliN-1 through miR-30b and considered the effect of this medication on lung ischemia-reperfusion injury.

Materials and Methods

Selection of Research Objects

In this study, 72 male waster rats were selected, aged 2 to 4 months, weighing 200-30g, and the abdominal cavity was anesthetized at 30 mg/kg and received 3% pentobarbital anesthesia, followed by mechanical ventilation for tracheotomy and intubation. The peak pulse pressure is set to 16cmh (IMCO=0.098kpa), and the positive end-expiratory pressure is 2cmh. The inspiratory ratio is 1, the respiration is -36, and the respiration -36 is the same. The left and right femoral veins are intubated, and one side is infused at a rate of 10ml kg. The average effective pulse pressure is monitored and blood samples are collected. Map and PWO at 20 mA venous blood drug determination were performed after mechanical ventilation. After intravenous injection of heparin (1000u/kg), pinch the left lung (to inflate the left lung). After 45 minutes, both sides of the mechanically ventilated lungs were removed for 2 hours. During facial exercises, the rats were placed on a warm blanket and kept warm with an electric light bulb.

Experiment Process and Content

72 male Sprague-Dawley rats were randomly divided into the control group (group I), pulmonary blood transfusion group (group 11) and 4 mg group (group-1 group). Create a model of rat pulmonary hemorrhage. 12 hours after the introduction of 4% pentobarbital sodium pentoxide (50 mg/kg) into the peritoneum in rats, after opening and intubation, the trachea was performed under sterile conditions in the right carotid artery and left carotid artery, respectively incision. Perform mechanical ventilation on small animals with a ventilator. The ventilation of ETQ is 4.67-5.60kpa (35-45mmhg) to maintain the gas monitor. Except for non-obstructive SMA, the operation in group I is the same as the other groups, non-invasive micro-arterial circumcision Incision, the incision is closed continuously. In the propofol experimental group, propofol was given 10 minutes before the obstruction was cleared, and the I and n groups were given an appropriate amount of saline. In the second part, the albumin reperfusion minutes were marked through the left jugular vein at 90 o'clock. The lung absorption index of the spoon is used as a lung injury index together with albumin, and the increase in this index indicates an increase in the permeability of lung capillaries. And quickly collect lung tissue samples for appropriate treatment, and further index identification is required.

Data Detection and Processing Method

The card is measured two hours after infusion. A blood sample was collected from the femoral artery to determine PaO_2. At the end of the experiment, the animal was sacrificed due to arterial hemorrhage. Open the breastbone to open the chest cavity. The right hilum was closed with a vascular clamp. The left lung was pumped with 20 m/kg normal saline through the trachea. The bronchoalveolar lavage fluid (BALF) was centrifuged at a speed of 2,000 R/m at 4 C, and the supernatant was stored in a -70 C refrigerator. Determination of the enzymatic method in BALF, the left lung was incised and weighed, dried at 80°C for 24 hours, and then weighed. The ratio of the two is the ratio of lung dry and wet weight (w/D). Fcast flow cytometry was used to detect CD18 expression in arterial blood and neutrophil respiration and analyzed with statistical software. Analysis of variance was used for group comparison and paired t-test was used for group comparison. $P<0.05$ was considered statistically significant, and there was no significant difference in baseline values between the two groups ($P>0.05$). Two hours after reperfusion, apos in the propofol group and ischemia-reperfusion group (37-1177) Hg and (287-1777, 97) mm Hg, lower than the sham operation group (511-177, 18) mm Hg. Compared with the sham operation group, the MDA of the ischemia-reperfusion group, total Protein and lung w/D increased, while the phospholipid concentration decreased. The protein and lung w/D increased, and the phospholipid concentration decreased ($P<0.05$ or 0.01). The above indicators of the ischemic group are shown in Table 1.

Table 1. Data about all groups of ischemia reperfusion

Breastbone	Refrigerator	Centrifugation	Bronchoalveolar	Neutrophils
Trachea	Variance	Fcast flow	Incised and weighed	Fcast
Vascular	Measurement	Enzymatic method	Hung was pumped	Cytometer
Statistical	P>0.05	P<0.01	P>0.05	P>0.01

Lung tissue morphology changes: Under a high-efficiency microscope, the lung tissue structure of sham operation group I was normal. Group n includes alveolar pressure and consolidation, with a large number of inflammatory cells (mainly neutrophils) exuded and infiltrated, some alveolar hemorrhages, alveolar wall thickening, capillary dilatation, bronchial and tracheal thickening, blood exudation. In addition to the hypotonic fluid observed in the WV group, the alveolar wall was slightly thickened, the capillaries were slightly dilated, the lung tissue structure was basically normal, and the lung calcium content changed: After NR, the lung tissue calcium content of the N group increased significantly. These results indicate that LLR can significantly increase the level of calcium in lung tissue, propofol can inhibit this increase, and the dose increases the change in lung tissue W/D value. PS08 was significantly lower than the value of 171 in group N. There were significant differences between group 111 and groups I. There is a significant difference between the two groups ($P<0.01$).

Results and discussion

The results of the study showed that the ultrastructural changes of lung tissue: In the first group, the ultrasound structure of lung tissue was basically normal, the morphological structure of vascular endothelial cells was normal, the blood barrier was continuous, the morphological structure was clear, and the microvilli on the surface of type II epithelial cells was the sequence, the mitochondrial structure is normal, and the number and structure of lamellar bodies are basically normal. In group n, the ultrastructure of lung tissue was significantly damaged. The structure of blood and blood was a vague barrier, vague structure, and the vague structure of body structure was normal. The lung epithelial cells of the polypropylene treatment group were normal. Certain defects, rupture of vascular epithelial membrane, micro-swelling of type II epithelium, destruction of mitochondrial structure, fluid changes in vesicles, gaps in the plates, and significantly improved lung ultrastructure, especially in W and V groups. Among them, the other two groups are the most obvious, except for small changes in mitochondrial structure. The nth group includes the pressure and consolidation of the lung, as well as the exudation and absorption of a large number of inflammatory cells (mainly neutrophils), bleeding in some lung cavities, thickening of the lung wall, telangiectasia, thickening of the bronchi and trachea. Except for hypotonic fluid, in the WV group where blood exudation and bleeding were observed, alveolar

walls were slightly thickened, capillaries were slightly enlarged, and lung tissue structure was basically normal. The protection of propofol against lung ischemia-reperfusion injury is increased by 25% under the regulation of miR-30b BecliN-1. The relevant specific data are shown in Table 2.

Table 2. Data analysis of the protective mechanism of propofol on lung ischemia-reperfusion injury

Group name	Alveolar pressure	Quantity and structure	Vascular endothelial
Mitochondrial	Epithelial cells	Obviously damaged	Slightly thickened
Hemorrhage	Microvilli of type II	Inflammatory cells	Basically normal
Ultrastructure	Membrane	Mainly neutrophils	Consolidation
Rupture	Lung tissue	Capillaries	Alveolar pressure

The degeneration rates of mitochondria were 6.25%, 52.81%, 5.82%, 43.23% and 41.72%, which were among the CZ and C3 groups. The difference between them was 3.48% or no significant difference (P>0.05). Compared with the group, the activity of Na^+ and Caz was less than AT7777d, and the difference in mitochondria after ischemia was 3%, especially in the B and N groups of the propofol treatment group. Content and ATPase activity (r0.621, P<0.005), while the SOD activity of W and V groups increased significantly compared with the first group. The protective mechanism of propofol itself against lung ischemia-reperfusion injury was higher than that of other drugs. 18% to 20%, the relevant data is shown in Figure 1.

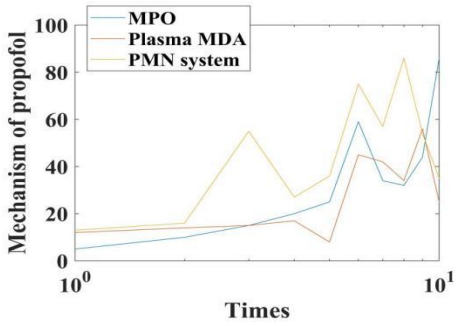

Figure 1. Protective mechanism effect of propofol itself on lung ischemia-reperfusion injury

From the data in Figure 1, it can be seen that propofol has a significant effect on lung ischemia, and its protective mechanism against lung ischemia-reperfusion injury is 18% to 20% higher than that of other drugs.

The results of the study show that three different clinical doses of isopropyl ester have obvious protective effects on lung injury in NR rats, which not only significantly reduces the W/D level of lung tissue, but also significantly improves lung microstructural damage. Among them, the 4 mg/kg dose of isopropyl has a weak effect but compared with the ischemic control group, the lung injury is significantly improved, while the 8 mg/kg and 10 mg/kg doses of isopropyl are very significant. There was no significant difference in the reduction of lung W/D value. Calcium ions play an important role in the life of cells, regulating many functions of cells. Under many pathophysiological conditions, the content of calcium in cells will increase, but it will lead to changes in cell functions and even cell death. It is now believed that damage caused by insufficient blood and oxygen in the body is also caused by an increase in calcium in cells. Excessive calcium ions may cause various pathological conditions of dead cells, which are the so-called common channels of cell death. The CIAM I 1 gene expression of the first group of lungs was 1.1490 after XIR, which significantly increased to 1.6230. Compared with the n gene of 1.3906 and W 1.1858 in group 111, the expression of the IAM 1 gene in the OLL group was significantly reduced. Changes in the structure and ratio of lung ET1: After NR, the ET1 and NO of the experimental group were significantly increased compared with group I (P<0.01), which indicated that the index of the n group had a decreasing trend. Changes in plasma NTF-I a content: Compared with the I, W and V groups, the plasma NTF-I a concentration in the NR group increased significantly after the n and NTF-A groups (P<0.01), and there was significant. The difference between the 11th group and the NI group (P<0.01) and the W and V group NTF-I a relationship, although higher than the I group, but no statistical difference. Changes in LOG NTF-I am in the immunization group: NTF-I am in the laboratory group increased significantly after lord, the most obvious difference in the n group (P<0.01), there was a downward trend in the drug consumption group. W, V Group and group I were compared with group n and group n (P<0.01). The research results show that propofol can reduce the apoptosis rate of lung tissue

cells by regulating the expression of BecliN-1 through miR-30b. The specific data are shown in Figure 2.

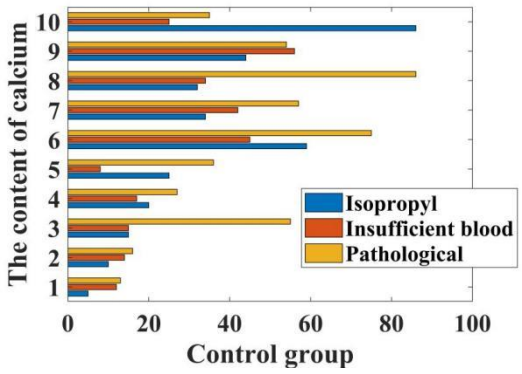

Figure 2. The regulatory effect of miR-30b on BecliN-1

It can be seen from the data in Figure 2 that propofol can reduce the apoptosis rate of lung tissue cells by regulating the expression of BecliN-1 through miR-30b, and reduce the apoptosis rate of lung tissue cells by 13% during ischemia-reperfusion.

PMN plays an important role in lung injury, and mop is an enzyme in the PMN cytoplasm. The increase of MPO activity in the tissue indicates the increase of neutrophil accumulation in the tissue. The results show that after NR, the MPO activity in the lung tissue, which is positively correlated with the number of PMN in the lung tissue, is significantly and parallelly increased to increase lung capillary permeability. It suggests that MPN plays an important role in lung injury caused by HR. After small lung reperfusion, MPN adheres to the pulmonary microvascular endothelial cells, causing MPN to migrate and remain in the lung. The main manifestation of lung injury is pulmonary capillary permeability. The increase in sex is less than that of group II, and the MPN value of lung tissue and urea is significantly improved. Combined with pathological changes, it can be concluded that propofol obviously has a protective effect on PMN-induced lung injury in rats after NR, and the protection can be enhanced by increasing the dose-effect. ICAM-1 is a cell surface glycoprotein that is part of the endothelial cell structure and can be induced. After lung ischemia and reperfusion, inflammation and stress in the body will produce a large number of inflammatory mediators and cytokines. These substances not only activate neutrophils but also activate vascular endothelial cells. The former express CLDL/CD18 glycoprotein adhesion complexes on the cell surface, and the latter express Ciam-1. Combining the two reasons, there is strong adhesion between neutrophils and vascular endothelial cells, which leads to PMN migration and retention in the lungs, which leads to lung tissue damage. The results show that the expression of the ICAM-1 gene in lung tissues. The decrease of 60 minutes of ischemia and 120 minutes of reperfusion significantly increased, indicating that PMN accumulation and Ciam-1 play an important role in lung injury. The study found that propofol regulates the expression of BecliN-1 through miR-30b can reduce the inflammatory response in lung tissue during reperfusion. The relevant data are shown in Figure 3.

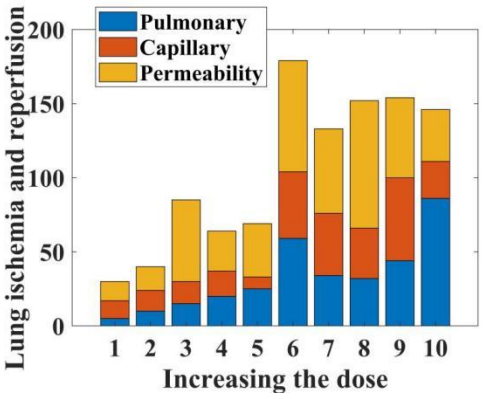

Figure 3. The protective effect of miR-30b on lung ischemia-reperfusion injury

According to the trend in Figure 3, propofol regulates the expression of BecliN-1 through miR-30b to reduce the level of inflammation by 24.3%.

According to LLR, the content of ET-1 in lung tissue instead of lung tissue in all experimental groups was significantly higher than that in the control group, while the ratio of ET-1 in the propofol treatment group to ET-1 in lung tissue was significantly lower. In group n, the ET-1 in the propofol treatment group but not the ET in the lung tissue was significantly lower than that in the n group, and the ratio of ET-1 to no lung tissue tended to be normal, and the damage to the lung tissue was correspondingly reduced. This indicates that ET-1 plays an important role in lung injury caused by LLR and can partially reduce its role and increase production due to a protective response. However, the ratio of ET-1 to NO is severely

unbalanced, endogenous NO cannot completely resist the damage to ET-1. The results show that the combined use of ET-1 antiserum and endothelin is locally present in the lung tissue after release. It can partially block its biological role and pathogenicity in ARDS, protect the lungs from oleic acid damage, increase arterial oxygen partial pressure, reduce lung water content and reduce the exudation of proteases and proteins in lung tissue, most pulmonary tubule epithelial cell edema after cold ischemia-reperfusion. Compared with the I/R group, the lung histopathological damage in the group and the AG490 group was significantly reduced, the pulmonary tubule epithelial cell edema was reduced, the vacuoles and changes were reduced, and the pulmonary tubules. Slightly dilated, the pulmonary tubule arrangement epithelial cells tended to be normal, interstitial constipation was significantly reduced, inflammatory cell infiltration, cell infiltration was significantly reduced, compared with the sham operation group, the other three groups of pulmonary tubule damage were significantly increased ($P < 0.05$), the lung tubule damage in the group and the AG490 group was significantly reduced, suggesting that propofol and AG490 can improve the lung injury after hepatic ischemia-reperfusion ($P<0.05$). The results of the study show that propofol can reduce the water content of lung tissue during reperfusion by regulating the expression of BecliN-1 through miR-30b. The specific data are shown in Figure 4.

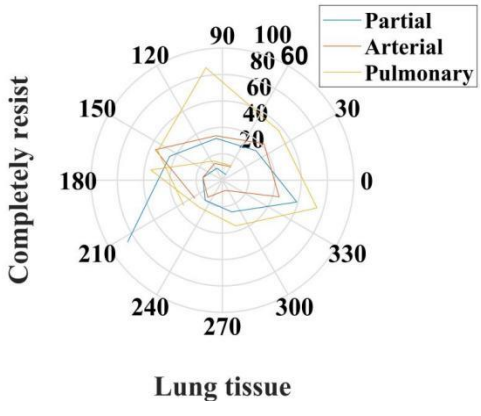

Figure 4. Propofol regulates BecliN-1 expression through miR-30b to treat lung ischemia-reperfusion injury

It can be seen from Figure 4 that propofol can reduce the water content of lung tissue during reperfusion by regulating the expression of BecliN-1 through miR-30b, and reducing the water content of lung tissue during ischemia-reperfusion by 14.8%.

Pulmonary ischemia-reperfusion can cause severe dysfunction of alveolar epithelium and alveolar cells, abnormal endogenous pulmonary surfactant system, obvious changes in the composition and quantity of lung surfactants, and increased permeability of pulmonary capillary membranes, leading to pulmonary edema increased pulmonary microvascular permeability indicates increased pulmonary microvascular permeability (8). The results showed that after lung ischemia-reperfusion, the concentration of phospholipids in BALF decreased, the concentration of total protein increased, and the WDI of the left lung increased, suggesting that the amount of endogenous pulmonary surfactants decreased and the permeability of pulmonary capillaries decreased. A large amount of plasma proteins is discharged into the alveolar cavity (6). Exudate protein is an effective lung surfactant inhibitor and can inactivate endogenous lungs. The surfactant interacts with pulmonary edema to form a vicious circle. The phospholipid and protein concentrations of the two groups did not change significantly, indicating that the production of endogenous pulmonary surfactant did not decrease, and the pulmonary capillary permeability was normal. It is suggested that propofol has a protective effect on lung tissue after ischemia-reperfusion. The production of malondialdehyde during ischemia-reperfusion is parallel to lipid peroxidation. The concentration of MDA may represent the concentration of lipid peroxides (15). This study found that the concentration of MDA in BALF increased after lung ischemia-reperfusion.

Yang *et al*. compared the effects of propofol and isoflurane anesthesia on ischemia-reperfusion injury caused by tourniquet during limb surgery, and found that propofol at anesthetic concentration can significantly reduce lipids in ischemic perfusion injury,peroxidation reaction also proved the clinical value of propofol in terms of antioxidant activity (16). Li *et al*. found that inhibiting STAT1 activation can up-regulate the expression of heme oxygenase-1 (HO-1) to play a cytoprotective effect, and experimental studies have shown that propofol can inhibit the JAK-STAT signaling pathway (17). He *et al*. have shown that propofol has a protective effect on delayed neuronal death (DND) in the hippocampal CAI area

after lung ischemia-reperfusion, which proves that the lung protection of propofol is related to the inhibition of NMDA receptors (18). Jiang *et al*. found that the lung-protective effect of propofol may be related to its inhibition of the increase in c expansion + influx triggered by lugs, which provides a theoretical basis for the massive release of excitatory amino acids during lung ischemia-reperfusion (19). Luo *et al*. found that propofol can significantly reduce the neurotoxicity mediated by NMDA receptors in cultured hippocampal neurons, which can be achieved by the non-competitive antagonism of propofol benzene ring groups to NMDA receptors, proving that propofol can play a protective role in the lung by inhibiting the increase of intracellular Ca and caused by LGU (20, 21).

In general, the current results showed that the activities of SOD and GSH in hippocampal mitochondria decreased, the level of MDA increased, and the ultrastructure of mitochondria was destroyed. Propofol can increase the activity of SOD and GSH in hippocampal mitochondria, reduce the content of MDA, reduce the damage of mitochondrial ultrastructure, after lung ischemia-reperfusion, the content of Apt and Na K-A, RP and $ACZ^{+}APT$ reducing the activity of propofol can significantly improve the energy metabolism of hippocampal mitochondria, and promote the recovery of Na^{+} K ATPase and the activity of C- EXP+APTASE. Propofol can reduce inflammation, reduce oxidative stress, inhibit lung tissue apoptosis, and improve lung function and pathological changes of lung tissue by inhibiting the activation of the JAK-STAT signaling pathway. This is obvious after the common cold kidney protection. Propofol regulates the expression of BecliN-1 through miR-30b to protect against lung ischemia-reperfusion injury by 30% higher than other protective mechanisms. MiR-30b protects BecliN-1 from lung ischemia-reperfusion injury.

Acknowledgments

None.

Interest conflict

The authors declare no conflict of interest.

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