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# Protective effect of magnesium sulfate on cranial nerves in preeclampsia rats through NF-κB/ICAM-1 pathway

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**Abstract. – OBJECTIVE: The aim of this study was to investigate the protective effect of magnesium sulfate (MgSO4) on the cranial nerves of preeclampsia (PE) rats through the nuclear factor-κB (NF-κB)/intercellular adhesion molecule-1 (ICAM-1) pathway.**

**MATERIALS AND METHODS: A total of 30 pregnant rats were randomly divided into three groups, including control group, model group, and treatment group, with 10 rats in each group. Systolic blood pressure was measured at 13 d, 15 d, and 19 d. The apoptosis level in brain tissues was detected *via* Western blotting and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay. Protein expression of genes was detected using immunohistochemical staining. Moreover, the messenger ribonucleic acid (mRNA) expressions of NF-κB and ICAM-1 in brain tissues were determined through Reverse Transcription-Polymerase Chain Reaction (RT-PCR).**

**RESULTS: Systolic blood pressure exhibited significant differences among the three groups at 15 d and 19 d of gestational age ($p<0.05$). At 15 d of gestational age, systolic blood pressure was significantly higher in model group than that of control group ($p<0.05$). However, it was slightly lower in treatment group than model group ($p<0.05$). At 19 d of gestational age, systolic blood pressure was significantly higher in model group than control group ($p<0.05$). However, it decreased remarkably in treatment group when compared with model group ($p<0.05$). In treatment group, systolic blood pressure at 19 d was significantly lower than that at 15 d ($p<0.05$). Subsequent Western blotting revealed that the protein expression of B-cell lymphoma-2 (Bcl-2) in brain tissues decreased evidently, whereas the expression of Bcl-2 associated X protein (Bax) increased significantly in model group compared with control group, showing statistically significant differences ($p<0.01$). The protein expression of Bcl-2 in brain tissues increased significantly, while the expression of Bax declined remarkably in treatment group compared with model group ($p<0.01$). The number of apoptotic cells in model group and treatment group increased significantly compared with that in control group, with the largest in model group ($p<0.05$). However, it remarkably declined in treatment group compared with model group ($p<0.05$). These results suggested that MgSO4 treatment could significantly reduce neuronal apoptosis in PE rats. According to the results of immunohistochemistry, the protein expressions of NF-κB and ICAM-1 in brain tissues were significantly higher in model group and treatment group than those in control group ($p<0.05$). However, they were significantly lower in treatment group than model group ($p<0.05$). RT-PCR results manifested that the mRNA expressions of NF-κB and ICAM-1 in brain tissues exhibited evident differences among the three groups ($p<0.05$). Model group and treatment group showed significantly up-regulated mRNA expressions of NF-κB and ICAM-1 in brain tissues compared with control group ($p<0.05$). The highest mRNA expression was observed in model group. However, treatment group exhibited remarkably decreased mRNA expressions of NF-κB and ICAM-1 in brain tissues compared with model group ($p<0.05$).**

**CONCLUSIONS: MgSO4 exerts a protective effect on cranial nerves of PE rats by inhibiting the NF-κB/ICAM-1 signaling pathway.**

*Key Words:*

Magnesium sulfate, NF-κB/ICAM-1 signaling pathway, Preeclampsia (PE), Cranial nerve, Protective effect.

## Introduction

Preeclampsia (PE) is a multi-system disease unique to pregnancy, with unknown causes[1]. It is mainly characterized by abnormal vascular response of the placenta, increased systemic vascular resistance, enhanced platelet aggregation, abnormal activation of the coagulation system, and endothelial dysfunction[2]. The clinical manifestations of PE include maternal syndromes

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(hypertension and proteinuria) or fetal syndromes (fetal growth restriction, amniotic fluid decrease, and oxygenation abnormality)[3].

In the 20th century, magnesium sulfate ($MgSO_4$) was the most commonly used effective drug for the prevention and treatment of PE. A large amount of empirical evidence[4] has confirmed the effectiveness of $MgSO_4$ in the prevention and treatment of eclampsia. In recent years, clinical studies have demonstrated that the therapeutic effect of $MgSO_4$ is superior to that of phenytoin sodium, nimodipine, and diazepam in PE women. Clinically, $MgSO_4$ reduces the risk of recurrent epilepsy by 52% in eclampsia patients compared with diazepam and by 67% compared with phenytoin sodium[5]. Although the effectiveness of $MgSO_4$ in the prevention and treatment of eclampsia has been widely elucidated, its mechanism of action still needs further exploration.

Currently, several mechanisms have been proposed by researchers to explain the neuroprotective effect of $MgSO_4$. Magnesium ions are a kind of calcium ion antagonist inside and outside cells, which can directly act on brain endothelial cells. As a calcium antagonist at the cytoskeletal actin level, $MgSO_4$ exerts a neuroprotective effect by affecting the paracellular motion at the tight junction and preventing the passage of solutes[6].

Nuclear factor-κB (NF-κB) is a transcription factor involved in the inflammatory response. It binds to the family of inhibitory proteins, inhibitors of NF-κB[7]. Many stimuli can activate NF-κB, including a variety of cytokines and reactive oxygen species (ROS)[8]. After the activation of the NF-κB signaling pathway, NF-κB subunits such as p65 and p50 will translocate to the nucleus. This may eventually regulate the expression of various inflammatory genes, including tumor necrosis factor-α, various cytokine receptors, cyclooxygenase-2, growth factor, and intercellular adhesion molecule (ICAM)[9,10].

NF-κB has been confirmed activated in many human diseases, including AIDS, atherosclerosis, rheumatoid arthritis, osteoporosis, Alzheimer's disease, and ischemia-reperfusion injury. These diseases are associated with increased oxidative stress and inflammation[11]. ROS induces the activation of NF-κB. In contrast, antioxidants inhibit the activation of NF-κB. Many studies have shown that the content of ROS is significantly up-regulated in PE. In addition, latest reports[12] have indicated that the NF-κB signaling pathway is abnormally activated in PE, thereby inducing cranial nerve death.

The aim of this study was to confirm whether $MgSO_4$ could significantly reduce the expressions of NF-κB and ICAM-1 in brain tissues, thus exerting a neuroprotective effect.

## Materials and Methods

### Objects of Study and Grouping

A total of 30 specific pathogen-free Sprague-Dawley rats weighing 200-250 g were provided by the Animal Experimental Center of Shanxi Medical University. All rats were randomly and equally divided into three groups, including control group (normal pregnant rats, n=10), model group (PE model rats, n=10), and treatment group (PE model rats treated with $MgSO_4$, n=10). They were normally fed under the ambient temperature of (23 ± 2)°C and humidity of 70%. This investigation was approved by the Animal Ethics Committee of Zhangqiu Maternal and Child Health Hospital Animal Center.

### Main Reagents and Instruments

Lipopolysaccharide (Sigma-Aldrich, Saint Louis, MO, USA), $MgSO_4$ injection (Shandong Linuo Kefeng Co., Ltd., Jinan, China), TRIzol reagent (Invitrogen, Carlsbad, CA, USA), polymerase chain reaction (PCR) primers (Olympus, Tokyo, Japan), desk horizontal centrifuge (Experimental Center of Guangxi Medical University, Nanning, China), medical ultra-low temperature refrigerator (Thermo Fisher Scientific, Waltham, MA, USA), optical microscope (Olympus, Tokyo, Japan), pathological image analyzer (Leica, Wetzlar, Germany), and NanoDrop2000 system (Thermo Fisher Scientific, Waltham, MA, USA).

### Establishment of Rat Model of PE and Extraction of Brain Tissues

In model group and treatment group, the rats were slowly injected with lipopolysaccharide solution (1 g/kg) *via* caudal vein at 14 d of gestational age to establish the rat model of PE. Rats in treatment group were treated with $MgSO_4$ (120 mg/kg/d) from 2 d before the termination of pregnancy. Meanwhile, rats in control group and model group were injected with 2 mL of normal saline for 2 consecutive days.

Rats in the three groups were decapitated at 20 d of gestational age, before which they were fed normally. After the rats were sacrificed, the skull was cut open and removed. Subsequently, brain tissues were completely stripped and fixed

with 4% paraformaldehyde. Brain tissues of 5 rats in each group were then randomly selected and embedded in paraffin. The remaining ones were stored in a refrigerator at –80°C for later use.

### Measurement of Systolic Blood Pressure in Each Group

Pressure gauge was first preheated till 38°C. The rats were fixed in the rat sleeve in a quiet and dark environment at 26-28°C. The tail was placed with the pressurized sleeve and pulse transducer. When the systolic blood pressure shown in the pressure gauge became stable, systolic blood pressure of tail was measured by one person in each group for 5 times at an interval of 2 min.

### Expressions of Apoptosis Proteins in Brain Tissues Via Western Blotting

An appropriate amount of radioimmunoprecipitation assay (RIPA) lysis buffer was prepared. Protease inhibitor phenylmethanesulfonyl fluoride (PMSF) (RIPA:PMSF = 100:1; Beyotime, Shanghai, China) was added and mixed evenly. After brain tissues were cut into pieces, the lysis buffer was added at 10:1. After complete homogenization using a tissue homogenizer, the lysate was collected and transferred into an Eppendorf (EP) tube (Hamburg, Germany), followed by centrifugation at 14,000 rpm and 4°C for 30 min. Protein supernatant was then collected and subjected to a heating bath at 95°C for 10 min for protein denaturation. Extracted protein samples were placed in a refrigerator at –80°C for subsequent use. The concentration of extracted protein was quantified using the bicinchoninic acid (BCA) kit (Beyotime, Shanghai, China). Protein samples were separated by dodecyl sulfate, sodium salt-polyacrylamide gel electrophoresis (SDS-PAGE) under the constant pressure of 80 V for 2.5 h, and transferred onto polyvinylidene difluoride (PVDF) membranes (Millipore, Billerica, MA, USA) using a semi-dry transfer method. The membranes were immersed in Tris-Buffered Saline Tween-20 (TBST) containing 5% skim milk powder and shaken slowly for 1 h on a shaking table to be sealed. After incubation with primary antibodies diluted with 5% skim milk powder, the membranes were rinsed with TBST for 3 times (10 min/time). On the next day, the membranes were incubated with corresponding secondary antibody at room temperature for 2 h, followed by rinsing again with TBST twice and with TBS once (10 min/time). Immunoreactive bands were developed using the enhanced chemiluminescence (ECL) reagent in the dark. Relative expression of the protein was analyzed using Image-Pro Plus v6 (Media Cybernetics, Silver Spring, MD, USA).

### Detection of Neuronal Apoptosis in Brain Tissues Using Terminal Deoxynucleotidyl Transferase-Mediated dUTP Nick End Labeling (TUNEL) Assay

Brain tissues were embedded, prepared into paraffin sections, and serially sliced into 5 μm-thick sections. The apoptosis of brain tissues in each group was detected *via* TUNEL assay according to the instructions. Five non-crossed and non-repeated fields were randomly selected from each pathological section and observed under an optical microscope. Light brown cells were apoptotic cells. The apoptotic rate of brain cells = number of apoptotic cells/total number of cells × 100%.

### Detection of NF-κB and ICAM-1 Protein Levels in Brain Tissues Through Immunohistochemistry

Protein expressions of NF-κB and ICAM-1 in brain tissues were detected through immunohistochemistry. First, brain tissues were prepared into coronal sections, deparaffinized and rehydrated, followed by antigen retrieval for 3 min. Then, the sections were rinsed with PBST and placed at room temperature for 10 min. After removing PBST, the sections were washed with PBS for 3 times (3 min/time). Next, they were sealed with 1% goat serum for 2 h and incubated with primary antibodies (1:300) at 4°C for 12 h. After primary antibodies were recycled, the sections were washed with PBS for 3 times (3 min/time) and incubated with secondary antibodies (1:300) at room temperature for 2 h. Then, they were washed again with phosphate-buffered saline (PBS) for 3 times (3 min/time), followed by color development using diaminobenzidine (DAB; Solarbio, Beijing, China) for 5 min. DAB was washed away with distilled water for 10 min, and hematoxylin was added dropwise for counterstaining, followed by photography.

### Detection of Messenger Ribonucleic Acid (mRNA) Expressions of NF-κB and ICAM-1 in Brain Tissues Via RT-PCR

The mRNA expressions of NF-κB and ICAM-1 in brain tissues were detected *via* RT-PCR. Tissue samples in the cryopreserved tube

were taken, drained, and ground with liquid nitrogen in 5 mL tubes. After complete homogenization using a tissue homogenizer, the liquid was transferred into a clean imported 1.5 mL EP tube and placed at room temperature for 5-10 min for complete lysis. After centrifugation at 1,200 rpm for 5 min, the precipitate was discarded. Chloroform and TRIzol (Invitrogen, Carlsbad, CA, USA) were added (200 μL of chloroform/mL TRIzol) to prepare the chloroform/TRIzol reagent, shaken and mixed evenly. Then, the mixture was placed at room temperature for 15 min and centrifuged at 12,000 rpm and 4°C for 15 min. The supernatant was aspirated into another centrifuge tube, added with isopropanol (0.7-1-fold volume of the supernatant), placed at room temperature for 10-30 min and centrifuged at 12,000 rpm for 10 min. The supernatant was discarded, and RNAs were precipitated to the bottom of tubes. Subsequently, 75% ethanol (1 mL of 75% ethanol/mL TRIzol) was added and gently shaken to suspend the precipitates, followed by centrifugation at 12,000 rpm and 4°C for 5 min. The supernatant was discarded as far as possible, and the precipitates were blown dry on a super clean bench for 10-20 min. Next, the precipitates were dissolved in 10-50 μL of diethyl pyrocarbonate-treated $ddH_2O$. The concentration of extracted RNA was detected using OneDrop micro-spectrophotometer. RT reaction was prepared, including 4.5 μL of RNase-free $ddH_2O$, 2 μL of 5×RT reaction buffer, 0.5 μL of random primers, 0.5 μL of Oligo dT, 0.5 μL of reverse transcriptase and 2 μL of RNAs. The complementary deoxyribonucleic acids (cDNAs) samples were divided into three pieces (diluted at 1:20), and 3 μL of cDNA was taken for PCR amplification. The amplification level of the target gene was verified *via* 5% agarose gel electrophoresis. LabWorks 4.0 image acquisition and analysis software was used for quantification and data processing. To obtain reliable data, the experiment was performed for three times. Primer sequences of NF-κB and ICAM-1 were shown in Table I.

### Statistical Analysis

Statistical Product and Service Solutions (SPSS) 20.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analysis. Three parallel groups were set up in each experiment, or the experiment was repeated for 3 times. Experimental data were expressed as mean ± standard deviation. The *t*-test was used to compare the differences among different groups. $p<0.05$ suggested that the difference had a statistical significance, and $p<0.01$ suggested that the difference had a remarkable statistical significance.

## Results

### Comparison of Systolic Blood Pressure Among the Three Groups

Systolic blood pressure showed statistically significant differences among the three groups at 15 d and 19 d of gestational age ($p<0.05$). At 15 d of gestational age, systolic blood pressure was significantly higher in model group than that in control group ($p<0.05$). However, it was slightly lower in treatment group than model group ($p<0.05$). At 19 d of gestational age, systolic blood pressure was significantly higher in model group than control group ($p<0.05$). However, it remarkably declined in treatment group when compared with model group ($p<0.05$). In the treatment group, systolic blood pressure at 19 d was significantly lower than that at 15 d ($p<0.05$) (Table II). The above results indicated that the rat pathological model of PE was successfully established in model group. Meanwhile, the therapeutic effect was better in treatment group.

**Table I.** Primer sequences.

| Gene | Primer | Primer sequences |
|---|---|---|
| NF-κB | F | 5'-GACCACTGCTCAGGTCCACT-3' |
| | R | 5'-TCATCTATGTGCTGCCTCGT-3' |
| ICAM-1 | F | 5'-CGAAGCTTCTTTTGCTCTGC-3' |
| | R | 5'-GTCCAGCCGAGGACCATA-3' |
| β-actin | F | 5'-CCTGGCACCCAGCACAAT-3' |
| | R | 5'-GCTGATCCACATCTGCTGGAA-3' |

**Table II.** Changes in systolic blood pressure of rats.

| Group | 13 d | 15 d | 19 d |
|---|---|---|---|
| Control group | 112.2 ± 4.5 | 108.5 ± 8.2 | 110.5 ± 8.2 |
| Model group | 111.5 ± 4.7 | 141.2 ± 8.2[a] | 139.2 ± 9.1a |
| Treatment group | 110.9 ± 4.8 | 138.9 ± 7.5[ab] | 119.9 ± 6.8[ab] |
| *F* | 0.876 | 26.758 | 165.040 |
| *p* | 0.668 | < 0.001 | < 0.001 |

*Note:* [a]$p<0.05$ *vs*. control group, [b]$p<0.05$ *vs*. model group.

### *Differences in Expressions of Apoptosis Proteins B-Cell Lymphoma 2 (Bcl-2) and Bcl-2 Associated X Protein (Bax) in Brain Tissues in the Three Groups Determined Using Western Blotting*

Western blotting revealed that the protein expression of Bcl-2 in brain tissues decreased significantly, while the expression of Bax increased markedly in model group when compared with control group, and there were statistically significant differences ($p<0.01$). The protein expression of Bcl-2 in brain tissues increased remarkably, while the expression of Bax declined evidently in treatment group compared with model group, showing statistically significant differences ($p<0.01$) (Figure 1). These findings indicated that $MgSO_4$ significantly reduced the protein expression of Bax and increased the protein expression of Bcl-2.

### *Neuronal Apoptosis in Brain Tissues in the Three Groups Determined Using TUNEL Assay*

The number of apoptotic cells in model group and treatment group increased significantly compared with control group ($p<0.05$), with the largest in model group. However, it remarkably declined in treatment group compared with model group ($p<0.05$) (Figure 2). All these findings suggested that $MgSO_4$ treatment could significantly reduce neuronal apoptosis in PE rats.

### *NF-κB and ICAM-1 Protein Expressions in Brain Tissues in the Three Groups Determined Using Immunohistochemistry*

According to the results of immunohistochemistry, the protein expressions of NF-κB and ICAM-1 in brain tissues were significantly higher in model group and treatment group than those in control group ($p<0.05$). However, they were significantly lower in treatment group than model group ($p<0.05$) (Figure 3). The above results demonstrated that $MgSO_4$ treatment significantly reduced the protein expressions of NF-κB and ICAM-1 in brain tissues of rats.

### *MRNA Expressions of NF-κB and ICAM-1 in Brain Tissues Detected Using RT-PCR*

RT-PCR results manifested that the mRNA expressions of NF-κB and ICAM-1 in brain tissues exhibited statistically significant differences among the three groups ($p<0.05$). Model group and treatment group had remarkably increased mRNA expressions of NF-κB and ICAM-1 in brain tissues compared with control group, with

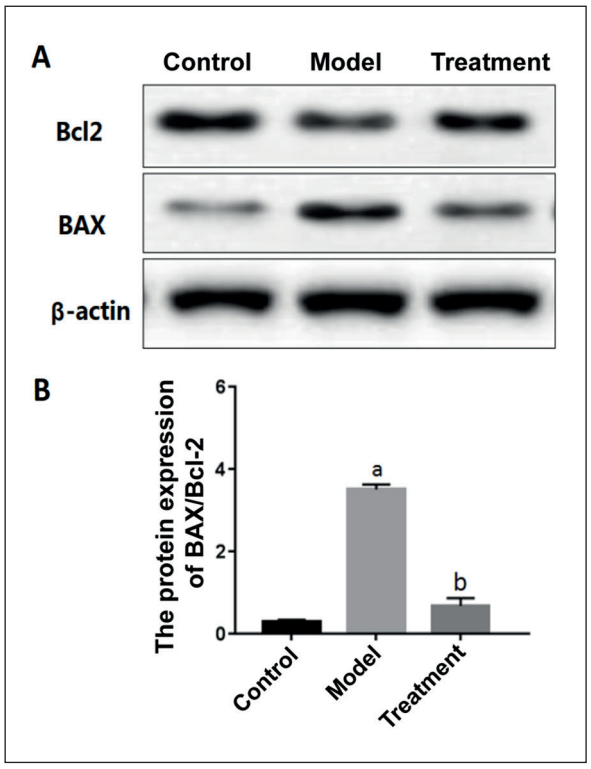


**Figure 1.** Expressions of apoptosis proteins in brain tissues in the three groups. **A,** Expressions of apoptosis proteins in brain tissues, **B,** Quantification of Western blotting results. [a]$p<0.05$ *vs.* control group, [b]$p<0.05$ *vs.* model group.

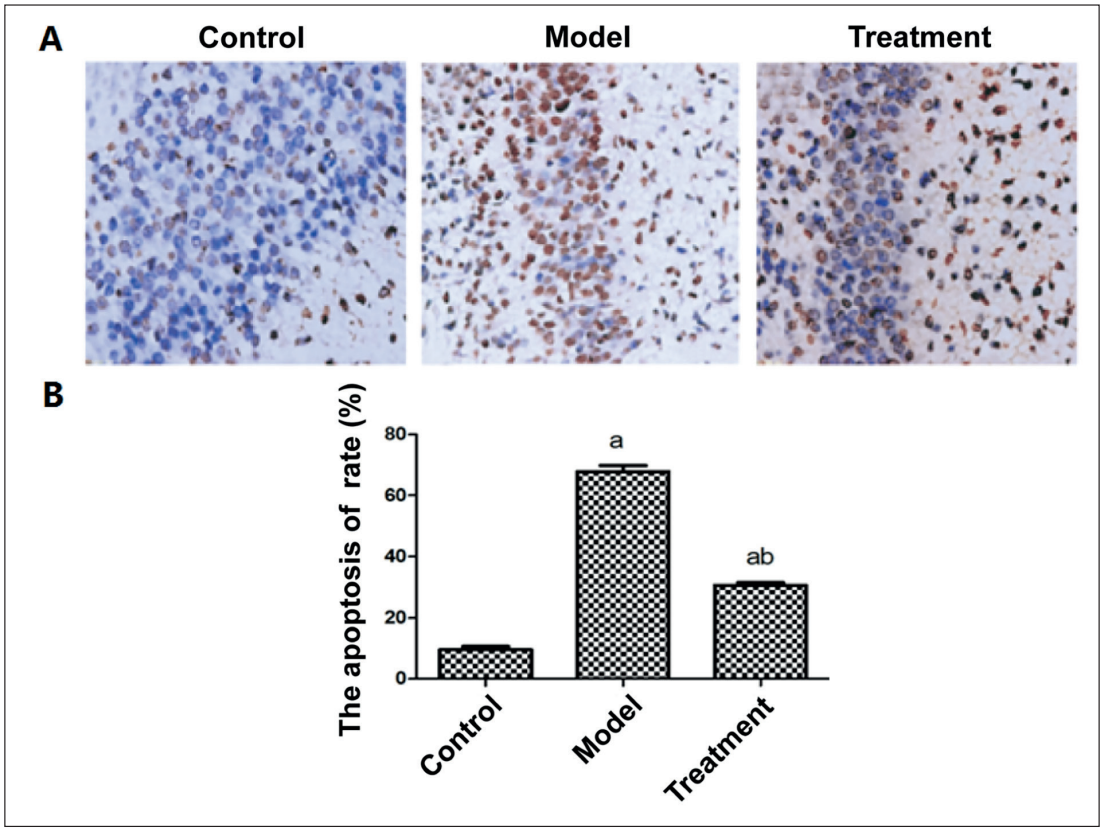


**Figure 2.** Apoptosis of brain tissues in the three groups. **A,** Apoptosis rate of brain tissues detected *via* TUNEL assay (magnification × 40), **B,** Quantification of TUNEL assay results. [a]$p<0.05$ *vs.* control group, [b]$p<0.05$ *vs.* model group.

highest mRNA expressions in model group ($p<0.05$). However, treatment group had significantly decreased mRNA expressions of NF-κB and ICAM-1 in brain tissues compared with model group ($p<0.05$) (Figure 4). All these findings suggested that $MgSO_4$ treatment evidently reduced the mRNA expressions of NF-κB and ICAM-1.

## Discussion

PE is a disease unique to pregnant women, as well as a common disease-causing neonatal death[9]. Vascular endothelial injury, vasospasm, and imbalance of redox reaction serve as important causes of PE. Inflammatory factors include the main signals of intercellular communication. Meanwhile, cytokines interact and coordinate with each other to maintain the intercellular balance. Toxins can activate PE. Therefore, the ideal rat model of PE was established using lipopolysaccharide in this research[13]. Cranial nerves are pairs of nerves on the left and right from the brain, which belong to the peripheral nervous system. Protein expression in cranial nerve cells is extremely important for the protection of the cerebral nervous system[14,15]. In the present study, systolic blood pressure showed significant differences among the three groups at 15 d and 19 d of gestational age ($p<0.05$). At 15 d of gestational age, systolic blood pressure was significantly higher in model group than that in control group ($p<0.05$). However, it was slightly lower in treatment group than model group ($p<0.05$). At 19 d of gestational age, systolic blood pressure was remarkably higher in model group than control group ($p<0.05$). However, it significantly declined in treatment group when compared with model group ($p<0.05$). In treatment group, systolic blood pressure at 19 d was significantly lower than that at 15 d ($p<0.05$). The above results indicated that the rat pathological model of PE was successfully established in model group. Meanwhile, the therapeutic effect was better in treatment group. In addition, the protein expres-

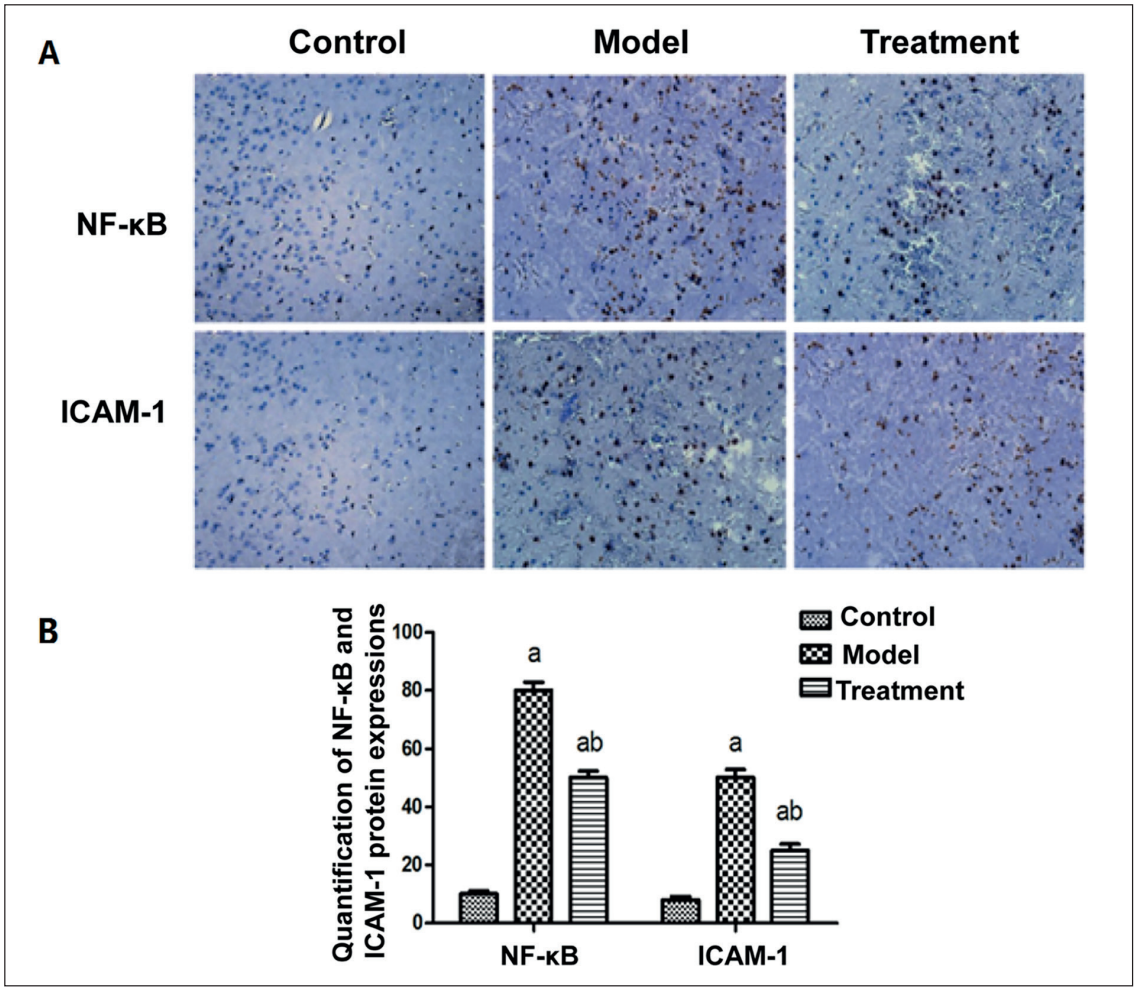


**Figure 3.** Protein expressions of NF-κB and ICAM-1 in brain tissues in the three groups. **A,** NF-κB and ICAM-1 protein expressions in brain tissues (magnification × 20), **B,** Quantification of NF-κB and ICAM-1 protein expressions in brain tissues. [a]$p<0.05$ *vs.* control group, [b]$p<0.05$ *vs.* model group.

sion of Bcl-2 in brain tissues evidently declined, while the expression of Bax increased significantly in model group compared with those in control group ($p<0.01$). The protein expression of Bcl-2 in brain tissues increased significantly, while the expression of Bax evidently declined in treatment group compared with model group, showing statistically significant differences ($p<0.01$). These results indicated that $MgSO_4$ could significantly reduce the protein expression of Bax and increase the protein expression of Bcl-2. TUNEL assay revealed that the number of apoptotic cells in model group and treatment group increased markedly compared with control group, with the largest in model group ($p<0.05$). However, it remarkably declined in treatment group compared with that in model group ($p<0.05$). All these findings suggested that $MgSO_4$ treatment could significantly reduce neuronal apoptosis in PE rats.

Currently, it is believed by most scholars that magnesium ions can protect the brain. Its protective mechanism may be related to the fact that many enzymes contain magnesium ions, which activates protective enzymes[16]. In recent years, the advantages of $MgSO_4$ have become ever more evident in obstetrics, which can replace diazepam and phenytoin in the treatment of eclampsia. At present, $MgSO_4$ is commonly used in the treatment of mild and severe PE. It has been found to inhibit the release of calcium ions from the sarcoplasmic reticulum through antagonizing the calcium channel of vascular smooth muscle. Therefore, myosin light-chain kinase is inactivated, and the contractility of smooth muscle

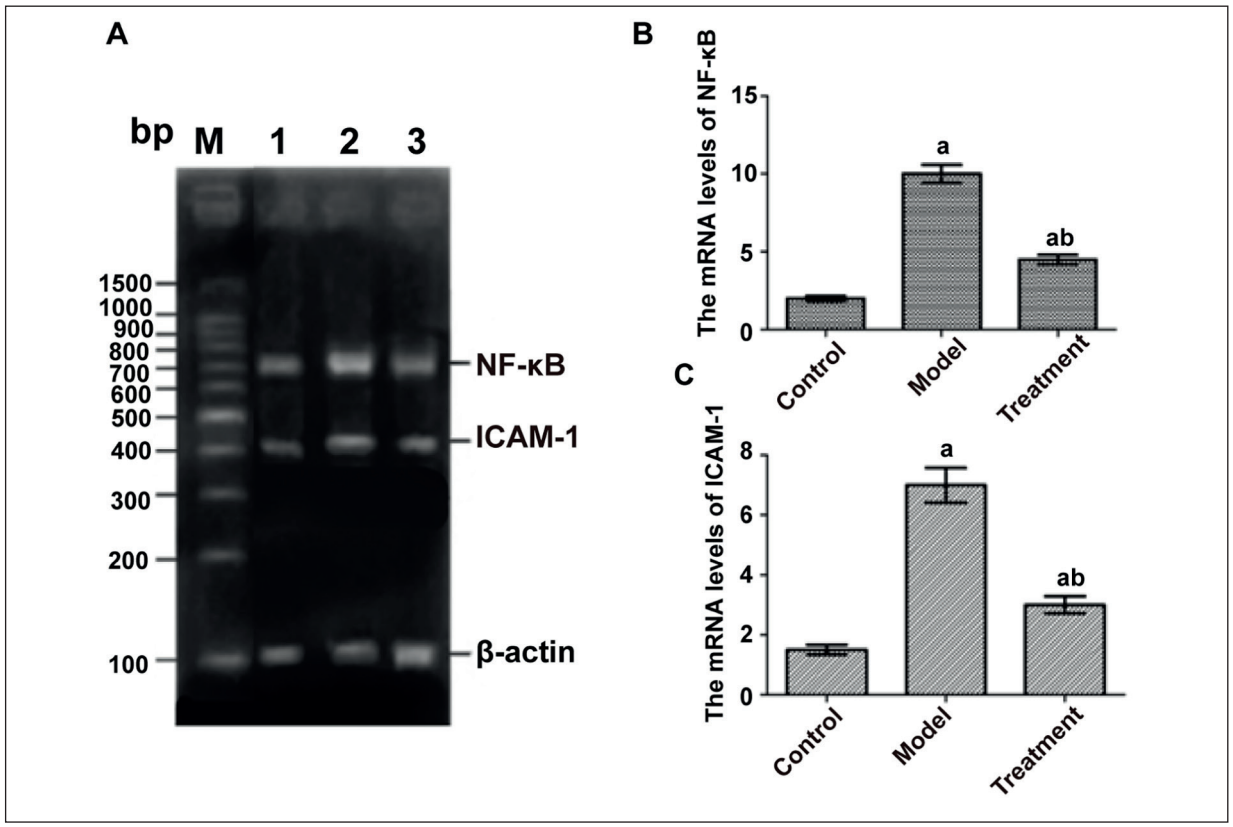


**Figure 4.** MRNA levels of NF-κB and ICAM-1 in brain tissues in the three groups. **A,** MRNA expressions of NF-κB and ICAM-1 in brain tissues, **B,** Comparison of NF-κB mRNA level in brain tissues, **C,** Comparison of ICAM-1 mRNA level in brain tissues. [a]$p<0.05$ *vs.* control group, [b]$p<0.05$ *vs.* model group.

declines, with vascular dilatation and drop of blood pressure[17]. Numerous researches have also demonstrated that $MgSO_4$ can reduce the level of angiotensin converting enzyme in the blood circulation. This results in decreased activation of endothelial cells and less production of vasopressin, thereby reducing blood pressure[18]. Currently, the mechanism of action of $MgSO_4$ has not been fully elucidated. In this study, our findings showed that $MgSO_4$ could effectively reduce the neuronal apoptosis of brain tissues, and remarkably down-regulate systolic blood pressure of rats. All these findings indicated that $MgSO_4$ had a certain protective effect in PE rats.

Immunohistochemistry demonstrated the protein expressions of NF-κB and ICAM-1 in brain tissues were significantly higher in model group and treatment group than those in control group ($p<0.05$). However, they were significantly lower in treatment group than those in model group ($p<0.05$). This demonstrated that $MgSO_4$ treatment reduced the protein expressions of NF-κB and ICAM-1 in brain tissues of rats. Our findings were inconsistent with the previous study[19]. Besides, RT-PCR manifested that the mRNA expressions of NF-κB and ICAM-1 in brain tissues exhibited evident differences among the three groups ($p<0.05$). Model group and treatment group showed remarkably increased mRNA expressions of NF-κB and ICAM-1 in brain tissues compared with control group, with the highest in model group ($p<0.05$). However, treatment group exhibited significantly decreased mRNA expressions of NF-κB and ICAM-1 in brain tissues compared with model group ($p<0.05$). The above findings suggested that $MgSO_4$ treatment evidently reduced the mRNA expressions of NF-κB and ICAM-1. NF-κB, a hub in the signal transduction pathway, is closely related to immune response. ICAM-1 is a member of the immunoglobulin superfamily, which mediates the tight binding between leukocytes and endothelial cells through binding to its ligand[20,21]. The NF-κB/ICAM-1 signaling pathway plays an important regulatory role in vascular endothelial cell injury induced by lipopolysaccharide and ischemia. The promoters

of ICAM-1 include the initiation site of NF-κB transcription, and its gene expression is regulated by NF-κB[22]. Activated NF-κB enters the nucleus and binds to the corresponding sites on DNA. Ultimately, this increases the protein expression of ICAM-1 and promotes inflammation. Therefore, inhibiting the expression of NF-κB could lower the expression of ICAM-1 and reduce the occurrence of inflammation, thereby exerting a protective effect on cranial nerves[23].

## Conclusions

We showed that $MgSO_4$ exerts a protective effect on brain tissues of PE rats through inhibiting the NF-κB/ICAM-1 signaling pathway. Our findings provide a new perspective for clinical diagnosis and treatment of PE.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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