ORIGINAL RESEARCH

Mechanism of Astragalus Injection to Relieve Symptoms of Preeclampsia Rat Model by Inhibiting MMP-9/sFlt-1/TNF-α

Quan Zhu, MM; Xia Wu, MM; Qingyun Long, BM; Ruixue Liu, MM

ABSTRACT

Objective • The aim of this study was to observe the effect of astragalus injection on rats with preeclampsia.

Methods • A total of 30 pregnant Sprague Dawley (SD) rats were randomly assigned to the model group (MG), the astragalus group (AG) or the control group (CG), with 10 rats in each group. The rat model of preeclampsia was established by subcutaneous injection of 50 mg/(kg·d) of N-nitro-L-arginine methyl ester (L-NAME), and 0.024 ml/(g·d) astragalus injection was administered intraperitoneally. The arterial pressure, urinary protein, placental mass, fetal weight, inflammatory factors in peripheral blood of pregnant rats, protein and mRNA levels of nuclear factor-κB (NF-κB), matrix metalloproteinase-9 (MMP-9), nuclear transcription factor 5 (NFAT-5), placental growth factor (PlGF), soluble fms-like tyrosine kinase-1 (sFlt-1), and reactive oxygen species (ROS) activity, malondialdehyde (MDA) and nitric oxide (NO) levels in placental tissues were compared in the 3 groups.

Results • After treatment, the arterial pressure and urinary protein levels in pregnant rats in the MG group were significantly higher than in the CG and AG groups ($P < .05$). The placental mass in the MG group was lower than in the CG and AG groups ($P < .05$). The messenger RNA (mRNA) and protein levels of sFlt-1, NFAT-5 and NF-κB, as well as ROS activity, MDA, inerleukin (IL)-6, tumor necrosis factor alpha (TNF-α) and interferon gamma (INF-γ) in the AG group were significantly lower than in the MG group, and mRNA and protein expression of MMP-9 and PlGF, as well as the NO level in the AG group, were significantly higher than in the MG ($P < .05$).

Conclusions • Astragalus injection can effectively inhibit the expression of sFlt-1, NFAT-5, NF-κB and enhance the expression of PlGF and MMP-9 in the placental tissue of rats with preeclampsia, which may be the mechanism of preeclampsia treatment. (*Altern Ther Health Med.* 2023;29(2):125-131)

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INTRODUCTION

Preeclampsia is a pregnancy-related condition and is the leading cause of maternal morbidity and mortality; surveys have shown that the prevalence of preeclampsia is 2% to 8% worldwide.[1] During the onset of this condition, patients often present with limb muscle rigidity and frequent convulsions; the prolonged duration of symptoms can lead to maternal coma, maternal and fetal death and preterm delivery. The pathogenesis and causes of this condition are still unclear in clinical studies, but several scholars have confirmed the theory of shallow placental implantation. Preeclampsia is a common complication during pregnancy.

It has been well documented that the progression of preeclampsia is, to some extent, closely linked to the expression levels of transcription factors such as matrix metalloproteinase (MMP)-9 and nuclear factor-kappa B (NF-κB).[2] MMP-9 is an important component of MMPs that can significantly affect the invasive ability of placental trophoblast cells during preeclampsia. Nuclear transcription factors (NTFs) are important transcriptional activators of several pre-inflammatory factors and play a key role in regulating the release of inflammatory factors at the transcriptional level. Placental hypoxia during pregnancy can promote NF-κB activation and inhibit the infiltration of trophoblast cells, causing vascular stenosis and inducing preeclampsia.

Astragalus injection (AI) is formulated using the active ingredients extracted from the traditional Chinese medicine (TCM) astragalus (AS), which can lower blood pressure, dilate blood vessels, enhance cardiac function, improve renal function and effectively reduce preeclampsia risk in pregnant

women.[3] To explore the effect of AI on preeclampsia treatment, we evaluated the effects of AI on the symptoms and MMP-9/soluble fms-like tyrosine kinase-1 (sFlt-1)/tumor necrosis factor alpha (TNF-α) pathway in a rat model of preeclampsia.[4-6]

MATERIALS AND METHODS

Reagents and Equipment

The astragalus injection (AI) was prepared from *Astragalus membranaceus* (Fisch) Bge. var. mongholicus (Bge.) Hsiao or *Astragalus membranaceus* (Fisch.) Bge. The effective purity of the sterilized aqueous solution extracted from the dried root of radix astragali was higher than 98%. The main ingredients include *Astragalus* saponins, *Astragalus* flavones, polysaccharide, etc, which contain 1 mg of astragaloside/ml, equivalent to 2 g of astragalus crude drug. AI (Specification: 20 mL, Z23020822) was purchased from Harbin Shengtai Pharmaceutical Co., Ltd. Shengtai, China and N-nitro-L-arginine methyl ester (L-NAME; 14H0135) was purchased from the Kaiman Company (Jingmei Biotechnology Co., Ltd. Chengdu, China). The urinary protease-linked immunosorbent assay kit, ABI7000 reverse transcriptase-polymerase chain reaction (RT-PCR) instrument, and supporting reagents were purchased from Shanghai Langfu Industrial Co., Ltd. (Shanghai, China).

Study Subjects

Sprague-Dawley (SD) rats with a gestation period of approximately 12 days were obtained from the Experimental Animal Center of Tongji Medical College, Huazhong University of Science and Technology in China. A total of 30 rats were included in the study. The rats were housed at a constant temperature of approximately 18°C to 26°C with 55%±5% relative humidity. It was a quiet environment with sufficient ventilation, and *ad libitum* food and water were provided. All applicable international, national and/or institutional guidelines for the care and use of animals were followed. This study was approved by Tongji Medical College, Huazhong University of Science and Technology, China.

Methods

A total of 30 pregnant rats were strictly selected and divided into the model group (MG), the astragalus group (AG), and the control group (CG) via the random number table method. Each group included 10 rats. To prepare rat models of preeclampsia, the MG and AG rats were subcutaneously injected on the 13th to 15th days of gestation with 50 mg/(kg/d) N-nitro-L-arginine methyl ester (L-NAME). The rat model of preeclampsia was successfully established;[7,8] the control group was injected with an equivalent amount of normal saline on the 13th to 15th days of gestation. The AG group was intraperitoneally administered 0.024 ml/(g-d) of AI on the 16th day of gestation, whereas the CG and MG groups were intraperitoneally injected with the same volume of 5% dextrose. Each group of rats received injections once a day for 5 days.

Outcome Measures

Detection of blood pressure and urine protein. Using the pyrogallol method, 24-hour urine samples were collected from each group on the 15th and 20th days of gestation and evaluated. Subsequently, the blood pressure of the rats in each group was measured noninvasively. A tail-cuff was placed on the tail to occlude the blood flow in a quiet environment to measure the arterial pressure. Each rat was tested once every 60 seconds, and the average of 3 measurements was considered the final value. On the 20th day of gestation, the rats were decapitated, and the placenta and fetus were removed to measure their weight.

Protein expression of NF-kappa B (NF-κB), matrix metalloproteinase (MMP)-9, nuclear factor of activated T-cells (NFAT)-5, placental growth factor (PlGF), and soluble fms-like tyrosine kinase-1 (sFlt-1). After collecting the 24-h urine samples, the rats were anesthetized by intraperitoneal injection with pentobarbital sodium (150 mg/kg). The rat placentas were washed with iced saline and stored at -70°C. The bicinchoninic acid assay (BCA) method was used for protein quantification. Proteins were separated using sodium dodecyl sulfate-polyacrylamide gel electrophoresis and subsequently transferred from the polyacrylamide gel to a membrane that was blocked with 5% skim milk. The membrane was incubated overnight with the corresponding primary antibody and β-actin as the internal control. The samples were incubated with immunoglobulin G (IgG) secondary antibody for 1 h, followed by treatment with enhanced chemiluminescence western blot detection reagent from G:BOX Chemi XRQ (Syngene, Bengaluru, Karnataka, India). The expression of NF-κB, MMP-9, NFAT-5, PlGF and sFlt-1 mRNA in the placental tissue was quantified using RT-PCR.

mRNA expressions of NF-κB, MMP-9, NFAT-5, PlGF and sFlt-1 using fluorescence quantitative PCR. The TRIzol method was used to extract total RNA from placental tissues, and Moloney murine leukemia virus reverse transcriptase was used to synthesize complementary DNA (cDNA). The primers were synthesized using Baocheng Biotechnology Co., Ltd., Hangzou, China to prepare a SYBR Green PCR Master Mix for quantitative analyses using PCR. The primer sequences for the NF-κB, MMP-9, NFAT-5, PlGF, and sFlt-1 genes are listed in the Table. The reaction conditions were 50°C for 2 min, followed by Taqase activation at 94°C for 30 s, 95°C for 15 s, and 60°C for 1 min over 40 cycles. The 2(-Delta Delta Cq) method was used to calculate the relative gene expressions.

Expression of inflammatory factors in peripheral blood and placental tissue. A total of 4 mL of peripheral rat blood was collected. After centrifugation, the plasma and placental tissues were homogenized and stored at -20°C. The expression of interleukin (IL)-6, tumor necrosis factor (TNF)-α, and interferon (INF)-γ in the plasma and placenta were determined using enzyme-linked immunosorbent assay (ELISA).

Reactive oxygen species (ROS) activity, malondialdehyde (MDA) levels and nitric oxide (NO) levels in placental tissues. The placental tissues were centrifuged at 4°C at 12,000 rpm for 30 min to obtain the supernatant. ROS activity was

Table. The Primer Sequences of Genes Used in This Study

Gene	Primer sequence
NF-κB	F: 5'-AACACTGCGAGCTCAAGAT-3'
	R: 5'-CATCGGCTTGAAAAGGAG-3'
MMP-9	F: 5'-CCT CTG GCA TCC TCT TGT TG-3'
	R: 5'-ACG CTG GTA TAA GGT GGT CT-3'
NFAT-5	F: 5'-CGACAGTGCCAAAGCACCTC-3'
	R: 5'-AACCGGATACTGTCCACACAACAT-3'
PlGF	F: 5'-GACTTCTGCTCACCCACGAG-3'
	R: 5'-CCCGGTGAGTTGGAGAGATG-3'
sFlt-1	F: 5'-GCACCTTGGTTGTGGCTGACT-3'
	R: 5'-GGGCCCGGGGGTCTCATTATT-3'
β-actin	F: 5'-GGCATCCTGACCCTGAGTA-3'
	R: 5'-AGGAAGGAAGGCTGGAAGAG-3'

Abbreviations: MMP, matrix metalloproteinase; NF-κB, nuclear factor kappa B; NFAT-5, nuclear transcription factor 5; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

detected using the thiobarbituric acid method. MDA and NO levels were detected using the Lucigen and nitrate reductase methods, respectively.

Statistical Analyses

The data were analyzed using Statistical Product and Service Solutions (SPSS) 19.0 (SPSS Inc., Chicago, IL, USA). The measurements were expressed as $\bar{x} \pm s$ and were compared using single-factor variance analysis. For the independent samples, t-test was used to compare the results in the 3 groups; $P < .05$ indicated a statistically significant difference.

RESULTS

Comparison of Arterial Pressure and Urine Protein Levels in the 3 Groups

On the 15th day of gestation, arterial pressure and urinary protein levels were significantly higher in the MG and AG groups than in the CG group ($P < .05$). On the 20th day of gestation, the arterial pressure and urine protein levels in the MG group were significantly higher than in the CG and AG groups ($P < .05$ and $P < .05$, respectively), suggesting that AI significantly reduced blood pressure and urinary protein levels in rats with preeclampsia (see Figure 1).

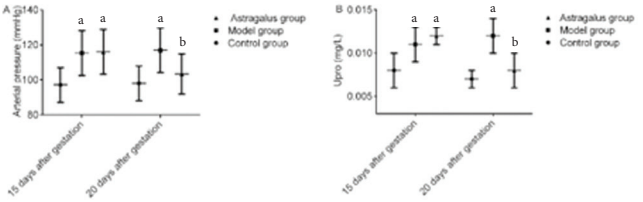
Comparison of Placental Mass and Fetal Weight

No significant difference was found in the fetal weight in the 3 groups ($P > .05$). The placental mass in the MG group was significantly lower than in the CG and AG groups ($P < .05$), indicating that AI could significantly improve the placental mass in pregnant rats with preeclampsia (see Figure 2).

Comparison of the Levels of Inflammatory Factors in the Peripheral Blood in Pregnant Rats

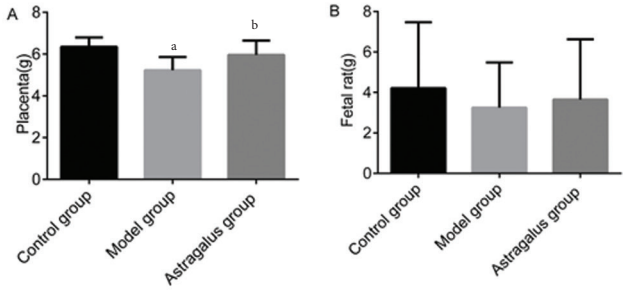
The peripheral blood levels of IL-6, TNF-α, and INF-γ in the MG group were significantly higher than in the CG and AG groups ($P < .05$, respectively), suggesting that AI could reduce the levels of peripheral blood inflammatory factors (see Figure 3).

Figure 1. Comparison of arterial pressure and urine protein levels at 15 and 20 days gestation in the 3 groups of rats. (**1A**) At day 15 gestation, arterial pressure and urine protein levels were significantly higher in the model and astragalus groups than in the control group; (**1B**) At day 20 gestation, arterial pressure and urine protein levels were significantly lower in the astragalus group than in the model group.



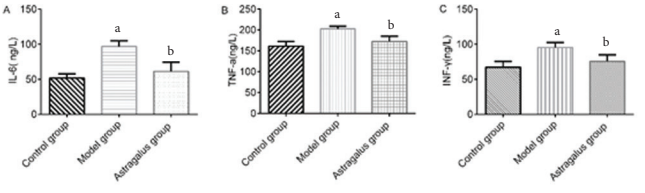
[a]$P < .05$, compared with the control group
[b]$P < .05$ compared with the model group

Figure 2. Comparison of placental mass and fetal body weight. (**2A**) Placental mass in the astragalus group was significantly higher than in the model group; (**2B**) there was no significant difference in fetal body weight between the 3 groups.



[a]$P < .05$, compared with the control group
[b]$P < .05$ compared with the model group

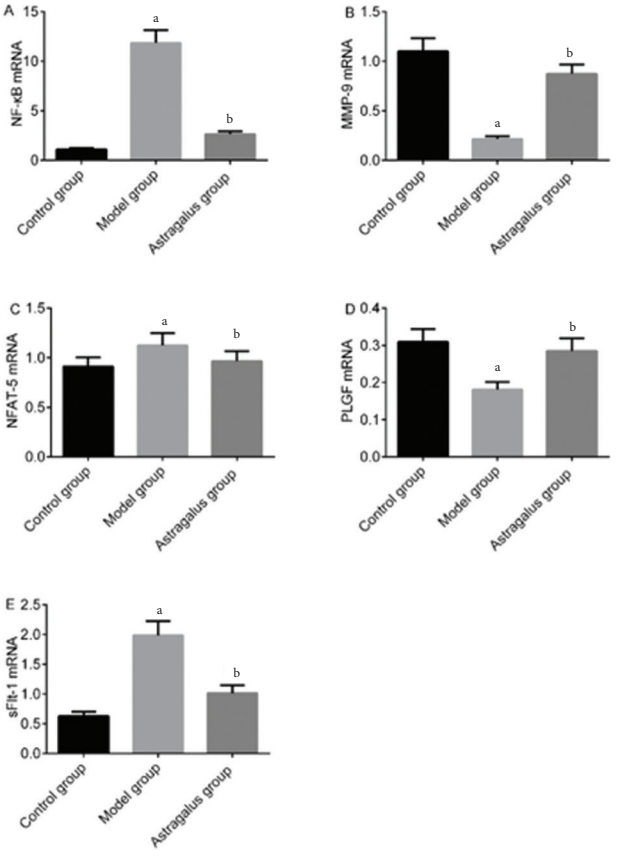
Figure 3. Comparison of the expression levels of inflammatory factors in the peripheral blood in the 3 groups of rats at 20 days gestation. (**3A**) The IL-6 level in peripheral blood of rats in the astragalus group was significantly lower than that in the model group; (**3B**) The TNF-α level in peripheral blood in rats in the astragalus group was significantly lower than in the model group; (**3C**) The INF-γ level in peripheral blood in rats in the astragalus group was significantly lower than in the model group.



[a]$P < .05$, compared with the control group
[b]$P < .05$ compared with the model group

Abbreviations: IL, interleukin; INF-γ, interferon gamma; TNF-α, tumor necrosis factor alpha.

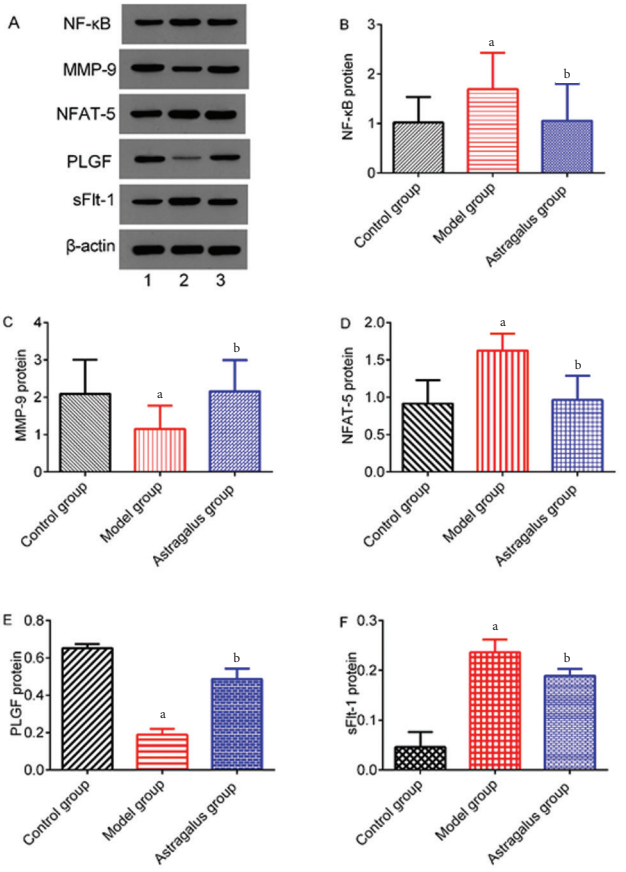
Figure 4. The expression levels of NF-κB, MMP-9, NFAT-5, PLGF, and sFlt-1 mRNAs in the placental tissues in the 3 groups of rats. (**4A**) The level of NF-κB mRNA in the placental tissue in the astragalus group was significantly lower than in the model group; (**4B**) The level of MMP-9 mRNA in the placental tissue in the astragalus group was significantly higher than in the model group; (**4C**) The level of NFAT-5 mRNA in the placental tissue in the astragalus group was significantly lower than in the model group; (**4D**) The level of PLGF mRNA in the placental tissue in the astragalus group was significantly higher than in the model group; (**4E**) The level of sFlt-1 mRNA in the placental tissue in the astragalus group was significantly lower than in the model group.



[a]$P < .05$, compared with the control group
[b]$P < .05$ compared with the model group

Abbreviations: MMP-9, matrix metalloproteinase-9; mRNA, messenger RNA; NF-κB, nuclear factor kappa B; PLGF NFAT-5, nuclear transcription factor 5; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

Figure 5. Comparison of the expression levels of NF-κB, MMP-9, NFAT-5, PLGF and sFlt-1 proteins in the placental tissues in the 3 groups of rats. (**5A**) The level of NF-κB protein in the placenta in the astragalus group was significantly lower than in the model group; (**5B**) The level of MMP-9 protein in the placenta in the astragalus group was significantly higher than in the model group; (**5C**) The level of NFAT-5 protein in the placenta in the astragalus group was significantly lower than in the model group; (**5D**) The level of PLGF protein in the placenta in the astragalus group was significantly higher than in the model group; (**5E**) The level of sFlt-1 protein in the placenta in the astragalus group was significantly lower than in the model group.



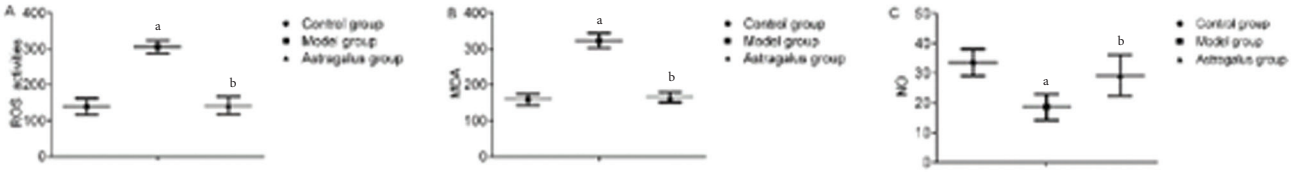
[a]$P < .05$, compared with the control group
[b]$P < .05$ compared with the model group

Abbreviations: MMP-9, matrix metalloproteinase-9; mRNA, messenger RNA; NF-κB, nuclear factor kappa B; PLGF NFAT-5, nuclear transcription factor 5; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1.

Comparison of mRNA Levels of NF-κB, MMP-9, NFAT-5, PlGF and sFlt-1 in Placental Tissues

mRNA expression levels of sFlt-1, NFAT-5 and NF-κB mRNA in the MG group were significantly higher than in the CG group, and mRNA expression levels of MMP-9 and PlGF mRNA were significantly lower than in the CG group ($P < .05$). The levels of sFlt-1, NFAT-5 and NF-κB mRNA in the AG group were significantly lower than in the MG group, and the levels of MMP-9 and PlGF mRNA in the AG group were significantly higher than in the MG group ($P < .05$). These data indicated that AI significantly decreased the levels of sFlt-1, NFAT-5 and NF-κB and increased the levels of MMP-9 and PlGF in placental rat tissue (see Figure 4).

Figure 6. Comparison of ROS activity, MDA and NO levels in the placental tissues in the 3 groups. (**6A**) ROS levels in placental tissues in rats in the astragalus group were significantly lower than in the model group; (**6B**) MDA protein levels in placental tissues in rats in the astragalus group were significantly lower than in the model group; (**6C**) NO levels in placental tissues in rats in the astragalus group were significantly higher than in the model group.



[a]$P < .05$, compared with the control group
[a] $P < .05$ compared with the model group

Abbreviations: MDA, malondialdehyde; NO, nitric oxide; ROS, reactive oxygen species.

Comparison of the Protein Levels of NF-κB, MMP-9, NFAT-5, PlGF and sFlt-1 in Placental Tissues

In the MG group, the protein levels of sFlt-1, NFAT-5 and NF-κB were significantly higher and the MMP-9 and PlGF levels were significantly lower than in the CG group ($P < .05$). In the AG group, the protein expression levels of sFlt-1, NFAT-5 and NF-κB were significantly lower and the MMP-9 and PlGF levels were significantly higher than in the MG group ($P < .05$), indicating that AI significantly reduced the levels of sFlt-1, NFAT-5 and NF-κB and increased the levels of MMP-9 and PlGF in the placental tissue in rats (see Figure 5).

Comparison of ROS Activity, MDA and NO levels in placental tissues

The ROS activity and MDA levels in the MG group were significantly higher and the NO level was significantly lower than in the CG group ($P < .05$). Furthermore, ROS activity, MDA levels and NO levels in the placental tissues in the AG group were significantly lower than in the MG group ($P < .05$) (see Figure 6).

DISCUSSION

We found that MMPs and their associated inhibitory molecules were involved in the regulation of cell invasion.[9] During gestation, multiple proteins interact and influence each other in dynamic equilibrium to ensure that the infiltration of trophoblast cells can meet gestational requirements and assist the full recasting of the blood vessels. Moreover, these proteins prevent excessive invasion of the endometrium and myometrium. MMPs are primarily involved in the degradation of the extracellular matrix, whereas MMP-2 and MMP-9 belong to a gelatinase family, and the products of their hydrolysis are V-type collagen and elastic fibers.[10,11] The NF-κB protein family is also crucial in regulating trophoblast invasion, and NF-κB is the most valuable immune response-regulating transcription factor in clinical immunology research.

In the cytoplasm, NF-κB is usually present in the nonliving state and mainly comprises P50/P65 and inhibitor of nuclear factor kappa B (IκB). NF-κB, on extracellular stimulation, phosphorylates IκB in the trimeric complex, eventually causing dissociation. Meanwhile, the NF-κB dimer moves from its cytoplasmic location in the nucleus and binds to the κB site, which is in the initiation factor region of the NF-κB-responsive genes, ultimately initiating gene transcription, via which the NF-κB regulates cytokines, chemokines and adhesion factors.[12,13] NF-κB is present in human trophoblast cells. During infiltration, trophoblast cells undergo adhesion, matrix dissolution and cell migration; matrix dissolution is an important step in the infiltration process, enhancing the clearance of physical barriers. Trophoblast cells themselves cannot dissolve substrates and phagocytose antigens. However, they can secrete substances such as MMPs and serine proteases that act on the extracellular interstitium. MMPs, which belong to a group of connective tissue proteases, can solubilize most of the extracellular matrix. Thus, MMPs play a key role in the processes of placental implantation, embryo implantation and uterine spiral artery remodeling.

AI is a herbal preparation with hypotensive effects. Studies have confirmed that astragalus application benefits the human body in various ways; for instance, it can enhance blood flow rate and glomerular filtration rate in the kidneys, thus reducing the damage caused by immune complexes to the glomerular basement membrane and facilitating the efficient removal of oxygen-free radicals and improving renal function.

SUMMARY

In summary, astragalus can increase urine volume and lower blood pressure.[14] This study demonstrated that the urinary protein and arterial pressure levels in the AG group were lower than in the MG group at 20 days gestation, indicating that AI treatment can reduce blood pressure and urinary protein levels, which is consistent with the data from a previous study.[15]

Trophoblast cells in rats have a low invasive capacity during preeclampsia, and a decrease in MMP-9 expression would weaken the invasive capacity of the uterine spiral artery, ultimately resulting in shallow placental implantation

and substantially decreased blood perfusion. Our study showed that the MMP-9 levels in the MG group were lower than in the AG and CG groups; the CG had the highest MMP-9 level. This result indicated that the treatment of rats with preeclampsia with AI could increase expression MMP-9, which is consistent with the conclusion of a previous report.[3]

Prolonged hypoxia in the rat placenta during pregnancy activates large amounts of NF-κB, impairing the infiltration of trophoblast cells and increasing the risk for vascular stenosis. When pregnant women have preeclampsia, their trophoblast cells undergo massive apoptosis, and levels of PLGF mRNA are low.[16,17] A study revealed that patients with preeclampsia had higher expression levels of sFlt-1 in their placental tissues than patients in the control group, suggesting that preeclampsia is associated with increased expression of sFlt-1.[18] The increased osmolarity of kidney cells in mice causes the heavy activation of NFAT-5. Furthermore, prolonged exposure to hypoxia causes a substantial increase in the risk for complications such as fetal growth restriction, preeclampsia and others, as well as overexpression of NFAT5 mRNA. This study showed that the expression of sFlt-1 and NF-κB was higher in the placental tissues of preeclamptic rats than in the CG and AG groups, indicating that AI could significantly increase the expression of sFlt-1 mRNA and NF-κB in placental tissues. These findings are consistent with the results of previous research.[19]

Our study showed that the expressions of NF-κB mRNA in the placenta of the MG and AG groups was significantly higher and that of MMP-9 mRNA was significantly lower than in the CG group. These results indicate that AI treats preeclampsia by decreasing the expression of NF-κB and increasing the expression of MMP-9, providing a novel reference for its clinical use in preeclampsia treatment. This study also found that AI could inhibit the expression of NFAT-5 mRNA and promote the expression of PlGF mRNA.

Immune tolerance dysregulation and inflammatory response are related to the occurrence of preeclampsia. IL-6 belongs to the IL-1 family, which can regulate the activity of pro-inflammatory factors and suppress local and systemic inflammation. During pregnancy, cytokines such as TFN-α and INF-γ, which are secreted by T helper type 1 (Th1) cells, inhibit the growth of the trophectoderm; that is, they inhibit the development of the placenta and damage the placental tissues. Together, INF-γ and TFN-α promote the activation and proliferation of natural killer (NK) cells, which can damage the embryonic tissue and inhibit the growth and development of the trophectoderm, embryo and fetus. Studies have shown that INF-γ interferes with placental growth and trophoblast reproduction, increases the risk for miscarriage and delays fetal development. In this study, the expression levels of IL-6, TFN-α and INF-γ in the MG group were significantly higher than in the CG and AG groups; thus, IL-6, TFN-α, and INF-γ levels were significantly higher in the rats with preeclampsia. Delaney, et al.[20] pointed out that the elevated IL-6, TFN-α and INF-γ levels in rats with preeclampsia damaged the trophoblast cells and affected the development of intrauterine fetuses, which would inevitably reduce the placental mass and fetal body weight in pregnant rats. Thus, consistent with the findings of Delaney et al., we found that AI could improve placental mass in rats with preeclampsia.

Patients with preeclampsia experience oxidative stress, which also impairs the development of preeclampsia.[21] ROS are exogenous oxidants, and elevated ROS levels due to oxidative stress can cause various cerebral diseases. ROS is effectively involved in placental cell growth, differentiation and apoptosis, and is a key factor that influences pregnancy outcomes. Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase has been found to be present in placental tissues during early gestation, and ROS levels were highest during this stage, indicating that ROS can influence the growth and development of placental blood vessels.

Currently, malondialdehyde (MDA) is a common indicator of oxidative stress; it is the end product of lipid substances following a peroxidation reaction. A study found that MDA levels are closely related to the onset of preeclampsia, as well as the severity of the condition; however, it has also been suggested that MDA levels are not significantly different between healthy pregnant women and pregnant women with preeclampsia. This result may be attributable to the different levels of MDA in the acquired samples. Moreover, MDA is an end product of the oxidation reaction of lipids, which can also be obtained via other pathways. In addition, the measurement of MDA can be influenced by several factors, resulting in low specificity and sensitivity. NO is a vascular diastolic factor synthesized using endothelial cells. Endogenous NO may induce the occurrence of preeclampsia. We showed that the ROS activity and MDA levels in the MG group were significantly higher than in the CG group, and the NO levels were significantly lower in the MG group than in the CG group, which was consistent with the above findings.

NF-κB can be activated in pregnant women by placental hypoxia. On one hand, it can hinder the infiltration ability of trophoblast cells; however, it can also cause some damage to trophoblast cells. Furthermore, it regulates the activation of endothelial cells in pregnant women, impairing the vascular function of endothelial cells and simultaneously releasing certain toxic factors that gradually narrow the blood vessels, hindering the placental vascular function in pregnant women. After the apoptosis of trophoblast cells, cytokine expression is induced, which promotes the phosphorylation of κB inhibitory protein and gradually enhances the relevant expression of cytokines, thereby promoting the production of vascular smooth muscle cells and increasing the thickness of the blood vessel wall. Both NF-κB and MMP-9 are involved in trophoblast erosion and placental vascular remodeling, and the abnormal expression of both largely causes preeclampsia symptoms.[22] This indicates that in patients who receive AI, NF-κB mRNA expression will be significantly lower and MMP-9 expression will be significantly higher than in patients who do not receive AI.

Study Limitations

Our study has certain shortcomings. First, the pregnant rats were randomly sampled. If the representation is insufficient, the research results are prone to deviation. Second, the number of rats in this experiment was small (only 30). The sample size must be increased to reduce experimental errors when evaluating similar factors in the future.

CONCLUSIONS

In summary, AI inhibited the expression of sFlt-1mRNA, NFAT-5 and NF-κB and increased the expression of PlGF mRNA and MMP-9 in the placental tissues of preeclamptic rats, which may be related to its mechanism in the treatment of preeclampsia.

CONFLICT OF INTEREST

None.

FUNDING

None.

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