MEDS Clinical Medicine (2022)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2022.030718
ISSN 2616-1907 Vol. 3 Num. 7

Research Progress on Establishment of Animal Model of Hypertension with Obstructing Phlegm-Dampness

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Keywords: Phlegm Dampness Obstruction Syndrome Animal Model, Research Progress of Membrane-Building Methods

Abstract: Phlegm-dampness accumulation syndrome is a common witness of many difficult clinical diseases, also known as phlegm-dampness interaction syndrome, etc. In traditional Chinese medicine, phlegm dampness is an important intermediate product in the occurrence and development of many hereditary diseases such as hypertension, coronary heart disease, and diabetes. As a tool to study clinical diseases, animal models need to simulate the pathological changes of human phlegm and dampness under the basic principles of syndrome differentiation and treatment in traditional Chinese medicine. In order to further study, this paper summarizes the animal models of phlegm dampness accumulation commonly used in current research and the animal models of hypertension syndrome combined with this syndrome and symptoms. To provide a basis for clinical diagnosis and treatment of syndrome differentiation.

Hypertension is one of the chronic diseases with elevated systemic circulation arteries. However, with the development and progress of society and the improvement of human living standards, hypertension is one of the main killers of cardiovascular and cerebrovascular diseases. According to the latest research data, the prevalence of hypertension among adults in China remains high and is increasing day by day [1]. The prevalence of hypertension is increasing year by year, and the population is getting younger and younger. Guidelines for Prevention and treatment of Hypertension in China, Trend chart, Figure 1 2018[2]. The results showed that with the increase of age, the prevalence of hypertension is increasing, which has attracted the great attention of many clinical researchers of traditional Chinese medicine. Due to the fast frequency of modern life, the imbalance of diet structure, young people's work and life pressure, lack of exercise and other reasons, the human body in phlegm damp evil air breeding, spleen loss of transport, accumulation of the body, phlegm wet sticky, a wet difficult to remove. Xin-mei li[3]. In the study of hypertensive patients, it was concluded that the proportion of phlegm dampness was the highest, which affected the TCM constitution of essential hypertension. However, H-type hypertension is the main type in Chinese hypertensive patients[4-5]. H hypertension is closely related to traditional Chinese medicine constitution, and it is most closely related to phlegm dampness. Phlegm dampness is an important pathogenic factor of obesity-induced hypertension. At present, there is no exact and unified understanding of the etiology and pathogenesis of hypertension in modern

medicine. At present, many doctors have conducted in-depth research on the etiology and pathogenesis of hypertension, and many theories believe that the main etiology and pathogenesis of hypertension is related to the phlegm-dampness knot. Zhu Danxi put forward "no phlegm, no dazzle" and believed that phlegm and dampness were closely related to this disease. Such as xue-jie han[6]. In recent years, phlegm dampness syndrome has become the focus of attention because of the "collateral disease theory" that phlegm dampness blocks the veins and narrows the lumen of blood vessels, causing the blood pressure to fall. In order to further study phlegm dampness obstructing hypertension, its related animal model is an essential research object. Therefore, this article reviews the research progress of animal models of hypertension with excessive phlegm-dampness.

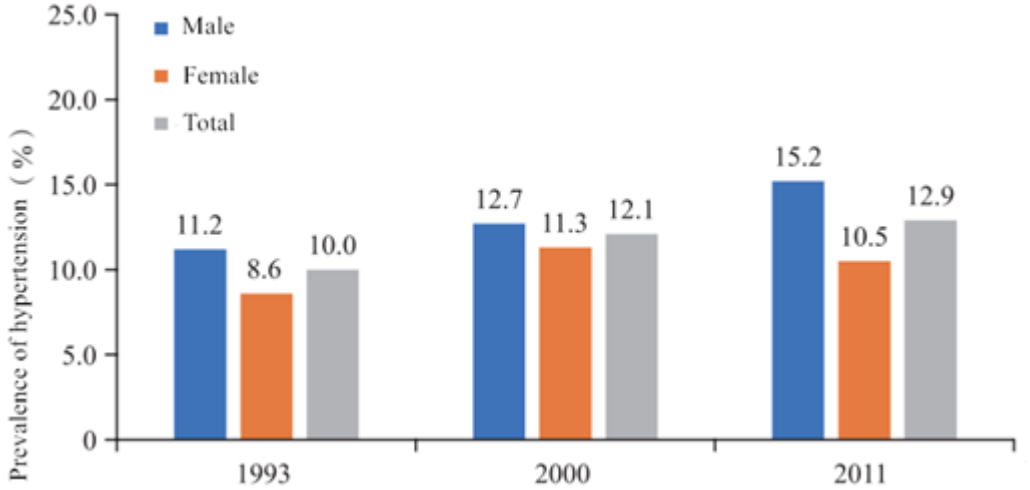

Figure 1: Trend chart.

1. Methods to Establish an Animal Model of Hypertension with Excessive Phlegm-Dampness

The syndrome of excessive phlegm dampness is one of the main syndromes of hypertension. There are many reasons for its formation, most of which are related to the patient's constitution. According to the diagnostic criteria of the syndrome of phlegm dampness accumulation in the Guiding Principles for Clinical Research of New Chinese Medicine (main syndrome: vertigo, headache, head congestion, chest tightness, vomiting, phlegm salivation, secondary syndrome: palpitation, insomnia, light mouth and little food, fat tongue, greasy moss, slippery pulse), the TCM said "Spleen is the source of phlegm" shows that the production of phlegm, accumulation and spleen operation ability is inseparable, spleen transport disorder, water is not wet, phlegm dampness in the obstruction. Secondly, Yang deficiency is an important factor in the formation of hypertension caused by excessive phlegm and dampness. With the growth of physiological age, the aging of body tissues and organs, kidney qi deficiency, kidney Yin and kidney Yang weakness to nourish spleen Yang, spleen loss of transport, water and grain are not refined, condensed into phlegm. Therefore, Yang deficiency is easy to produce phlegm and dampness. Pang An Chang of the Song Dynasty once said: "Those who treat phlegm well do not treat phlegm but qi." Miscellaneous diseases Guangyao": "People with qi deficiency and obesity, phlegm dampness on the upper, Yin fire starts from the lower, is with phlegm and empty fire, the head of the upper rush, positive qi can not win the enemy, so Qi deficiency is easy to produce phlegm dampness. Gu Jianxia[7] Professor Gu concluded that the pathogenesis of dampness obstructing summary shown in Figure 2 hypertension is mainly related to poor diet, generating dampness and eliminating phlegm. 2. Lao Is injury to the spleen, difficult transportation of fluid and essence, phlegm

production and obstruction; 3. Liver depression, body fluid is not good, sputum and wet; 4. Endowment element is weak or old weak, easy to produce wet sputum. In conclusion, there are many inducements for the formation of hypertension with excessive phlegm dampness, which are mainly related to the loss of spleen health, insufficiency of qi and qi, and the lack of true Yang in the elderly. In the animal model of hypertension induced by phlegm-dampness accumulation, it was found that most animal models were prepared by diet induction and etiological simulation in SHR rats, and the diet-induced animal model could also be summarized as the etiological and pathogenesis induced animal model. At present, the animal model of phlegm-dampness accumulation in hypertensive rats is mainly prepared in the following ways:

Pathogenesis of hypertension	1.Disordered diet, dampness and phlegm	2. Tired thinking hurt the spleen, subtle difficult to transport, sputum obstruction	3.Mood paralysis, body fluid is not good, phlegm produced wet;	4.Endowment factor weak or high body weak, poly wet phlegm

Figure 2: Summary of hypertension pathogenesis.

1.1. Diet Disorder, Producing Dampness and Phlegm

ZangYuHan [8], In the modeling method of spleen deficiency and phlegm turbidity syndrome animal model and model evaluation, "single factor or compound factor Table of single and compound factors Figure 3 modeling method was selected. Based on the basic theory of traditional Chinese medicine, the spleen is the main transport, digestion, absorption and transportation of water and grain and water liquid from the spleen to the whole body, and the nourishment of the five viscera and six Fu organs of the whole body and the skeletal muscles. The spleen can reabsorb, transport and transport water and liquid to prevent water and liquid from staying in the body. If the spleen is not healthy, the water valley and water fluid function will be seriously injured, which will affect the water valley transport and water fluid distribution. Thus, there is a saying that "phlegm arises from the middle". Therefore, the animal model of hypertension induced by dietary irregularity can be summarized as a single factor[9] Sugar, fat and protein are the main energy sources in high sugar diet. The ratio, calculated in terms of calories, is about 3:1:1 for drinking 1.5% NaCl solution (prepared with distilled water) without limit, 2.2. Feed with high-fat diet[10]. And in Li Qin[11] "Exploring the protective mechanism of Jianpi Huatan Prescription on vascular endothelium in piglets with hyperlipidemia and spleen deficiency and phlegm turbidity based on S1PR1/PI3K/Akt/eNOS signaling pathway" feeding piglets with high-fat feed to establish phlegm-dampness obstructing body. The high fat diet formula contained cholesterol 3%, pig bile salt 1%, peanut oil 6%, lard 6%, and basic feed 84%.Feeding method: high fat diet feeding frequency twice a day, feeding time 8:00 am, 16:00 PM, according to the weekly weight of pigs, adjust the feeding amount), free drinking water.3. High-salt feed feeding[12], NaCl saline plus regular feed feed.4 Feed with high purine feed[13]. The outbred group (SD) rats were fed continuously with the following diet proportions: ordinary feed, yeast dry powder, and adenine were prepared according to a certain ratio, 5.5. Compound feeding. Fan Jing taken[14]. In the research progress of high fat, high glucose, and high salt induced metabolic syndrome combined with an animal model, C57 mice induced by high fat, high glucose, and high salt diet were used to construct the syndrome of high metabolic syndrome. The model group mice showed phlegm dampness accumulation syndrome. Chen Teng Dumpling[15] and others in "build and analysis

evaluation of dietary induced spontaneous hypertension phlegmy wet type indicates sheng rat animal model" of experimental animals were given common feed, high fat feed, feed and high fat and sugar high fat and salt feed, compared with the control group, model group induced by high fat and salt phlegmy wet type indicates sheng hypertension animal model of rats syndrome differentiation of traditional Chinese medicine is more close to the edge, model the success rate is high, The mortality rate was lower, the experimental operation was simple, and the survival rate was higher. It is suggested that the animal model of hypertension induced by high-fat and high-salt diet has the most clinical characteristics of the natural course of human hypertension.

hypertension	Single factor film-making method	Composite factor modeling method
Disordered diet,dampness and phlegm	1. High sugar feeding 2. High fat feed 3. High salt diet 4. High purine diet	High fat, high sugar and high salt

Figure 3: Table of single and compound factors.

1.2. Fatigue Injures the Spleen and Causes Sputum Obstruction

Based on the traditional Chinese medicine theory that spleen is acquired, "the source of qi and blood biochemistry" and "the spleen is the source of sputum production", Xu Yulian [16] in the experimental study of a rat model of hypertension with Qi deficiency and phlegm turbidity, SHR rats were selected to fast every other day and swim to exhaustion. The animals were overworked and fed high-fat diet every other day. The main formula of high-fat diet was ordinary feed, sugar, cooked pig, and milk powder, with a ratio of 14:4:2:1.Lead to temper damage, transport and chemical grain fine function decline. So brew phlegm turbidity, phlegm from the middle.

1.3. Emotional Failure, Body Fluid is not Transported, Sputum Produced Wet

Figure 4: Mode of stimulation.

According to the function of "liver main dispersing", it is manifested as regulating mental emotions, helping the spleen to promote digestion and absorption, maintaining the transport of qi, blood and body fluid, etc. When the liver is lost, the Qi, blood and body fluid do not run smoothly, and the body fluid accumulates and produces sputum. In Jiang Xiudong [17] Through chronic stimulation combined with high-fat diet feeding in human SHR rats, a rat model of liver stagnation and phlegm-blocking hypertension was successfully established. Chronic stimulation: the rats were tied with their hind legs and hung upside down in the cage to irritate the rats, which showed obvious anxiety and biting. Each stimulation lasted for 20 minutes, and the stimulation was increased by 10 minutes every week (Mode of stimulation figure 4).

1.4. Weak Endowment Hormone, Damp and Phlegm.

SHR rats have stable hypertension heritability, and the elevated blood pressure is mostly related to genetic inheritance. Its pathogenesis is highly similar to that of human hypertension. Hypertension belongs to "vertigo tinnitus" and other categories in traditional Chinese medicine. According to the basic theory of TCM syndrome differentiation and treatment, Tan Wei [18] in the study of improving cerebral vascular adaptive regulation function in spontaneously hypertensive rats with Yiqi Huatan prescription, Tan Wei et al. "gave spontaneous Yiqi Huatan prescription to rats for gavage treatment. Yifang verified that SHR rats belong to the type of phlegm-dampness hypertension. The results showed that Yiqi Huatan can improve the cerebral vascular adaptive regulation function of SHR rats, and can supply blood continuously when the fluctuation of blood pressure is small. These results indicated that Yiqi Huatan Decoction could improve the adaptive regulation function of cerebral blood vessels, stabilize blood pressure and maintain cerebral blood supply in rats.

2. Summary and Discussion

At present, modern medicine to the etiology and pathogenesis of hypertension standard has not yet have a clear and unified, no one is put forward by the doctor of traditional Chinese medicine, hypertension disease, high blood pressure in the Chinese medicine analogy for diseases such as "vertigo, tinnitus, according to the disease often points to syndromes of traditional Chinese medicine, high blood pressure can be divided as phlegmy wet type indicates sheng, liver Yang syndrone type, gore block, Yin and Yang are two virtual type, etc. Hypertension can be divided into phlegm-dampness accumulation type, liver-yang hyperactivity type, congestion block type, yin-yang deficiency type, etc. In order to establish the animal model of hypertension in accordance with the clinical syndrome, the animal model combining disease and syndrome is often adopted. Phlegm-dampness obstructing hypertension is the most closely related to human constitution, which is called the focal syndrome of hypertension in traditional Chinese medicine research. SHR rats, SD rats, W rats, rabbits, miniature pigs, and so on can be used in the establishment of animal models of hypertension with excessive phlegm dampness. The selection of animal models is an important tool for clinical experiments. Advantages and disadvantages of common animal models Comparison of advantages and disadvantages, Figure 5, rats are the first choice for a large number of clinical experimental research models, especially SHR rats, which are the most frequently used model animals. Due to its physiologically stable inheritance of hypertension, elevated blood pressure is influenced by polygenic inheritance, and its pathogenesis, adaptive regulation of peripheral vascular resistance, salt sensitivity, and complications are surprisingly similar to those of human hypertension. Therefore, SHR has been adopted as the first choice for the study of an animal models of hypertension. Other animals, such as miniature pigs, have a high price, which is not conducive to large-scale experimental feeding. Rabbits are herbivorous animals, and long-term feeding may lead

to food rejection. The most commonly used model of hypertension induced by excessive phlegm dampness is established by diet induction. The animal model of excessive phlegm dampness, dampness induced by high fat and salt model group is more consistent with the characteristics of syndrome differentiation and classification of traditional Chinese medicine, with higher modeling rate and lower mortality. The model mice showed the symptoms of sluggish movement, lethargy, lethargy, laziness, lack of drinking water, and irregular stool. The blood lipid level was elevated, insulin resistance occurred, and blood pressure was generally elevated. In addition to the genetic model of hypertension, there are many methods to establish the animal model of hypertension, but there are still great controversy. For example, surgical preparation or drug enticement can easily cause the death of experimental animals. The animal model of hypertensive phlegm dampness accumulation established by the above methods has the clinical characteristics of hypertension, and there is still a long way to go to study its pathogenesis and the natural course of hypertension in humans.

Animal model of hypertension	SHR rats	The rabbit	Miniature pig
Pros and cons	Advantages: Stable heredity of hypertension, elevated blood pressure is related to multi-gene heredity, its pathogenesis, peripheral vascular resistance changes, salt sensitivity and complications are highly similar to human hypertension. Disadvantages: More expensive	Advantages: High survival rate, easy to feed. Disadvantages: large size, herbivorous animals, long-term feeding feed easy to cause rejection	Advantages: Cardiovascular structure is most similar to that of humans, and is often used for cardiovascular research Disadvantages: Small pigs make experiments more expensive and not conducive to large-scale experiments.

Figure 5: Comparison of advantages and disadvantages of commonly used animals.

References

[1] Wang J, Wang F, Liu H, Ye P, et al. A national survey on the incidence, awareness, treatment and control rates of hypertension in China. The Chinese journal of hypertension, 2015, 23 (3): 298. DOI: 10.16439 / j.carol carroll nki. 1673-7245.2015.03.029.

[2] Wang Zengwu, Chen Zuo, Zhang Linfeng, Wang Xin, Hao Guang, Zhang Zugui, Shao Lan, Tian Ye, Dong Ying, Zheng Congyi, Wang Jiali, Zhu Manlu, Weintraub William S,Gao Runlin. Status of Hypertension in China: Results of the China Hypertension Survey from 2012 to 2015. Circulation, 2018, 137(22): 131-136.

[3] Li XM, Qiujie. Analysis of traditional Chinese medicine constitution characteristics and related influencing factors

in patients with essential hypertension. Journal of Integrated Traditional Chinese and Western Medicine Cardio-Cerebrovascular Diseases, 2021, 19(13):2138-2141.
[4] Zhao T B, Wang X Z, Wen Y P, et al. Analysis of the characteristics of traditional Chinese medicine constitution in 210 patients with H-type hypertension. Chinese Journal of Contemporary Medicine, 2021, 28(24):188-191.
[5] Yan Lei. H high blood pressure and the correlation of TCM constitution research. Shandong university of Chinese medicine, 2020, DOI: 10.27282 /, dc nki. Gsdzu. 2020.000638.
[6] Han X J, Shen N, et al. The influence of toxin on the heart collateral and hypertension.Chinese Journal of Traditional Chinese Medicine (BMJ) 2005 BMJ 46 (2): 155-156.
[7] Gu J X, Gu J X. Experience summary of treating hypertension with excessive phlegm-dampness mound from the perspective of physique. Chinese Journal of Ethnic Folk Medicine, 2021, 30(10):91-92+96. (in Chinese). 10.13193 DOI: 2910 / j.i SSN. 1673-7717.2018.12.021.
[8] Zang Yuhan, Zhang Huiyong, Min Dongyu, et al. Pixu (spleen deficient) phlegm turbidity syndrome animal model building methods and the research progress of model evaluation. Journal of practical internal medicine of traditional Chinese medicine, 2021, 35 (07): 21-25. DOI: 10.13729 / j.i SSN. 1671-7813. Z20210370.
[9] Wang Y, Zhang Y L, Zhang Y L. Hypertension TCM syndrome with acute cerebrovascular disease types of correlation study. Journal of guiyang college of traditional Chinese medicine, 2002 (3): 58-60, DOI: 10.16588 / j.carol carroll nki issn1002-1108.2002.03.040.
[10] Xia Xiaoli. Establishment and characteristics of metabolic syndrome animal model in spontaneously hypertensive rats //2011 · Proceedings of Chinese Medical Doctor Association Congress of Integrated Traditional and Western Medicine Physicians. [Publisher unknown],2011:696-700.
[11] Li Q, Zhang H Y, Zhou H, et al. Study on the protective mechanism of Jianpihuatan decoction on the vascular endothelium of piglets with hyperlipidemia and phlegm turbidity based on S1PR1/PI3K/Akt/eNOS signaling pathway. Chinese Journal of Traditional Chinese Medicine, 2021, 36(08): 4564-4567.
[12] Wang Q, Zhang Y, Zhu Y, Wang Y, et al. A preliminary study on the high expression of soluble epoxidease in renal tissue of high salt-induced hypertension rats. Journal of Peking University Medical Sciences, 2010, 42(02):126-130.
[13] Zhang Q, Lu Q Y, Xia C Q, et al. Long-term high purine diet induced hypertension animal model. Journal of traditional Chinese medicine pharmacology and clinical, 2013, 29 (01): 159-162. The DOI: 10.13412 / j.carol carroll nki zyyl. 2013.01.056.
[14] Fan Jingyi. Study on the combination of disease and syndrome in animal model of metabolic syndrome induced by high-fat, high-glucose and high-salt diet. China Academy of Chinese Medical Sciences, 2018.
[15] Chen Teng-jiao, Xu Nan. Spontaneously hypertensive phlegmy wet type indicates sheng rat animal model building and analysis of evaluation. Journal of pharmaceutical research, 2015 (9): 503-506. The DOI: 10.13506 / j.carol carroll nki JPR. 2015.09.003.
[16] Xu Y L, Wang Q H, Zheng H L, et al. Deficiency of phlegm turbidity animal model to study hypertension in rats. Journal of traditional Chinese medicine new drug and clinical pharmacology, 2017, 28 (02): 196-201. The DOI: 10.19378 / j.i SSN. 1003-9783.2017.02.011.
[17] Jiang XD, Gu Wanli, Lv Bowei, et al. Establishment and evaluation of rat model of liver hypertention and phlegm-obstruction hypertension (English). Modern biomedical progress, 2012, 12 (4): 608-611. The DOI: 10.13241 / j.carol carroll nki PMB. 2012.04.017.
[18] Tan W, Liu P Y, Lin L, et al. Effect of Yiqi Huatan decoction on cerebral vascular adaptive regulation in spontaneously hypertensive rats. New traditional Chinese medicine, 2019, ploidy (07): 10.