Research Progress in Pharmacology of Semen Strychnine

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Abstract: Brucine and strychnine are the main components of semen strychnine, which affects the inflammation, central nervous system and immune system of human body. In addition, semen strychnine also significantly inhibits the early and secondary lesions of adjuvant arthritis in rats. At the same time, it can only affect the cellular immunity while other immune functions are normal. In addition, semen strychnine also influences the respiratory, cardiovascular and digestive system, and owns very good resistances function to cancer. However, the components of semen strychnine are a kind of toxic ingredients, so the toxicity and treatment amount are comparatively close. After actual poisoning, it is very likely to lead to systemic lesions of central nervous system. Even in severe cases, muscles of the whole body may also appear tonic spasm, which will inhibit the myocardium and respiratory muscles to a certain extent, leading to death. Therefore, in actual clinical practice, it is necessary to strictly control the measurement and pay more attention to compatibility and processing, so as to improve the rationality of use.

1. Introduction

Semen strychnine mainly is the mature seed of Yunnan nux vomica or nux vomica plants, which distributes in subtropical and tropical areas. Semen strychnine contains 1.5% to 5% alkaloids, in addition to a small amount of vomicine, loganin, icajine, novacine and so on, the main component of which is strychnine, followed by brucine. It tastes bitter and cold, with great toxicity. Its main efficacy is to dredge collaterals, relieve pain and dissipate nodules and swelling, so it is commonly used for carbuncle, swelling and pain, rheumatism, fall injury, numbness and paralysis, etc. Semen strychnine enjoys a history of nearly a thousand years in clinical application, with very remarkable effect. At the same time, because it belongs to a kind of poison, its application is also limited.

2. Pharmacological Effects of Semen Strychnine on Nervous System

Brucine and strychnine are the main components of semen strychnine. They are not only effective but also toxic components. The most toxic one is strychnine. An adult who takes about 7 mg strychnine orally may lead to poisoning. Up to now, the research on strychnine has been quite thorough. The sodium and potassium currents can be effectively blocked at the nodes of ranvier of frog and the axon of squid. The whole central system can be stimulated by strychnine, which further excites the vascular motor center and respiratory center of medulla oblongata, stimulates the reflex function of the spinal cord, and significantly improves the sensory center function of the cerebral cortex. After the respiratory center and vagus nerve are excited, breathing will be accelerated and deepened. In addition, strychnine can also excite the cough center [1]. In a case of relatively large dose of strychnine, it will appear over-limit inhibition after a short excitation. If the dose is relatively small, the excitation process of cortex will be effectively strengthened. A rapid awakening of patients in the depressed state can be promoted. Moreover, the functions of various sensory organs such as vision, hearing and touch can also be effectively improved. Strychnine tastes bitter, so the reflex of taste receptors will be greatly increased, and gastric juice will increase, so that appetite and digestion can be effectively promoted.

The content of brucine in semen strychnine is second only to strychnine. At the same time, its toxicity is much less than strychnine. Sensory nerve endings will be paralyzed by semen strychnine.

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When the dosage is very large, the transmission of nerve and muscle will be blocked. On this basis, it shows the effect of arrow poison. By recording the free-moving brain wave of mice, we can find that mice are not only affected by brucine, but also inhibited by brucine. The occurrence of these two effects is closely related to the dosage of drugs and drug sensitivity of animals to a certain extent. According to relevant studies, brucine has a much stronger central analgesic effect than strychnine. Morphine can not only increase the analgesic effect through brucine, but also prolong the analgesic time effectively. By studying the central analgesia mechanism of semen strychnine, we can find that it is directly related to the specific content of enkephalin and the increase of monoamine neurotransmitters in brain[2]. However, it is found that brucine alone can easily induce analgesic tolerance, so it can be combined with morphine in general. The time of morphine analgesic tolerance will be effectively delayed. In addition, there is no addiction to brucine, which is of great guiding significance for clinical practice.

3. Pharmacological Effects of Semen Strychnine on Cardiovascular System

3.1 Antiarrhythmia

The activity of L-type, T-type and B-type single channels in cardiac myocytes of Wistar rats can be stimulated by brucine. Their specific opening time has been prolonged a lot, and their closing time has been greatly shortened. The open probability increases without seriously affecting the ion flow amplitude of each ion channel. The electron microscopic observation of isobrucine nitrogen oxides and isobrucine showed that they could effectively counteract the damage of ultrastructural effects on cultured mitochondria and myofibrils caused by xanthine oxidase-xanthine. In addition, it was found that semen strychnine and the nitrogen oxides of semen strychnine can not only increase blood flow, but also improve microcirculation. Drug administration in vivo can effectively prevent thrombosis.

Myocardial calcium channel can be effectively blocked by brucine, because brucine significantly affects the slow response action potential induced by histamine with high potassium ion and isoprenaline in isolated guinea pig papillary muscles, and has a close relationship with its concentration. Adrenaline was intravenously injected into rabbits, aconitine into rats, chloroform or calcium chloride intraperitoneally into mice. On this basis, the arrhythmic model was established. The arrhythmic maintenance time, the incidence of ventricular fibrillation and the latency of arrhythmia in saline group and brucine group were also studied. By contrast, it was found that arrhythmia was often antagonized by brucine.

3.2 Antithrombotic Effects

By observing the effects of antiplatelet aggregation produced by brucine nitrogen oxides and brucine thrombosis, it was found that when compared with aspirin, adenosine diphosphate at the same concentration is actually more similar to aspirin in inhibiting platelet aggregation induced by brucine nitrogen oxides. In addition, if the actual dose of brucine has reached half of aspirin and brucine nitrogen oxides, its effect is the same as that of aspirin and brucine nitrogen oxides.

4. Pharmacological Effects of Immune Response and Inflammation

The inflammation of adjuvant arthritis rats will be affected by brucine. It can be observed that brucine dose at 10 mg/kg did not produce a serious impact on the weight of immune organs, but it effectively and obviously inhibited the immune organs. The changes of hemagglutinin antibody content caused by immunity of sheep red blood cell and the phagocytosis function of mouse macrophages were not affected by compound strychnos Tablets. However, the delayed hypersensitivity in mice and secondary injury in adjuvant arthritis in rats at different stages were significantly inhibited. Cellular immunity as well as the hypersensitivity of body to immune complexes were inhibited selectively, but in fact there was no extensive immune mechanism. Therefore, in the actual treatment of rheumatoid arthritis, it is a very ideal drug.

In addition, through the research of relevant scholars, it is known that the total alkaloids also

own a good anti-inflammatory effect. Strychnine, as a toxic component, is also an ineffective component. In the study, alkaloids were extracted from semen strychnine, and then separated again, and strychnine was separated. The non-alkaloids and the total alkaloids removed from part of strychnine and strychnine were separated altogether. It was also found that rat foot swelling could be effectively inhibited by the total alkaloid fraction and the tissue proliferation of rat granulation was significantly inhibited. In addition, the non-alkaloid and strychnine had no effect on the above-mentioned inflammation.

Moreover, some scholars have separated the extract of semen strychnine and studied it separately. Through the study, we know that both festrychnine alkaloids and the powder of semen strychnine could effectively inhibit the swelling of feet and soles. About five hours after the actual administration, the swelling of feet and soles was significantly inhibited, but for strychnine and non-alkaloids, there was no effect ($P < 0.05$). Through the experimental study, it was found that the powder of semen strychnine can effectively play an anti-experimental arthritis role, and festrychnine alkaloids are the effective part [3]. The transdermal absorption of toxic components in animal blood and the specific permeability of toxic components in traumatic tincture in vitro were measured by high performance capillary electrophoresis. The intensity of transdermal absorption of toxic components in vivo and in vitro was measured by this method. The vivo method showed that aconitine was not detected in the blood of rabbits in high dose group, and strychnine was not detected in the blood of rabbits in low dose group. This indicates that strychnine can be transdermally absorbed to a certain extent in vivo or in vitro, but not aconitine. Finally, it is known that strychnine with strong toxicity is an ineffective component, while strychnos alkaloids play an important role in anti-rheumatoid and arthritis. According to the research, strychnine has no anti-inflammatory effect. It can be removed by separating and processing active ingredients or extracting festrychnine alkaloid monomer in anti-inflammatory compound prescription, which will not affect the actual effect, but effectively reduce toxicity.

5. Pharmacological Effects of Antitussive, Analgesia, Expectorant, Antiasthetic and Inhibiting Tumor

Relevant scholars have recorded sodium currents in rat hippocampal CAL pyramidal neurons by using whole-cell patch clamp technique, and then observed the specific effects of brucine on sodium currents. According to relevant research results, sodium current was reversibly inhibited by brucine concentration-dependent manner. Therefore, the main analgesic mechanism means that sodium current is blocked by brucine, and the decoction of brucine has different inhibitory effects on microbacterium auduri and trichophyton schulandrae in vitro. At the same time, according to in vitro experiments, the growth of diplococcus pneumoniae, haemophilus influenzae, catarrhalis and group A streptococcu could be effectively inhibited by 0.1% brucine. Mitosis of lymphocyte were effectively inhibited by high concentration of brucine decoction, but it promoted the mitosis of lymphocyte when its concentration was relatively low.

In addition, by comparing the effects of isobrucine nitrogen oxides and brucine on antioxidant damage and anti-tumor cell growth in vitro, we can know that isobrucine nitrogen oxides had very good antioxidant and anti-tumor cell growth effects, but brucine’s effect was not very obvious. Moreover, the specific effects of brucine on the lymphocyte function of mice showed that the lymphocyte of mice could be regulated by the function-dependent immunity of brucine in analgesic dose. Therefore, it can be concluded that strychnine nitrogen oxides, strychnine and brucine can effectively inhibit the morphological damage and overall growth of cancer cell lines. The specific mechanism may be the inhibition of protein synthesis in cancer cells.

6. Conclusion

In a word, the treatment with brucine excites the reflex function of spinal cord, as well as the vasomotor center and the respiratory center in the medulla oblongata. On this basis, the function of cerebral cortex sensory center can be improved, and the respiratory center will be severely inhibited

by the amount of poisoning. For strychnine, it can effectively prevent the destructive effect of cholinesterase on acetylcholine, which will strengthen the intestinal peristalsis of patients.

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References

[1] Liu Xuemin, Wang Xiaoming, Zhao Jinling, Pang Chunxue, Zhu Yunliang. Chemical Constituents and Pharmacological Effects of Semen Strychnine [J]. Inner Mongolia Traditional Chinese Medicine, 2013, 32 (14): 52-53.

[2] Lu Yanhua, Gao Ningyang. Research Progress in Pharmacological Effects and Methods of Reducing Toxicity and Synergism of Brucine [J]. Shanghai Journal of Traditional Chinese Medicine, 2019, 53 (05): 93-97.

[3] Shen Jiaqi. Study on the Preparation Process of Brucine Cataplasm [J]. Heilongjiang Science and Technology Information, 2016 (21): 49.

[4] Tan Liuping, Yang Ke, Zeng Chunhui. Advances in Modern Processing Methods of Semen Strychnine [J]. Modern Chinese Medicine, 2018,20 (07): 906-909+914.

[5] Zhang Qungang, Zhang Qunxia, Zhang Yan. Pharmacology, Toxicology and Safety of Semen Strychnine [J]. Modern Diagnosis and Treatment, 2012, 23 (09): 1422-1423. [J].

[6] Zhu Longtao, Gong Qianfeng, Yi Bingxue, Ren Jianfeng, Yuxiang. Research Progress on Processing, Chemical Composition, Pharmacology and Toxicology of Semen Strychnine [J]. Journal of Jiangxi College of Traditional Chinese Medicine, 2012, 24(03): 98-100.