

Research Progress of Traditional Chinese and Western Medicine on Tic Disorder in Children

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Abstract: Children's tic disorder is a neurodevelopmental disorder that begins in childhood, which is characterized by muscle contraction, that is, involuntary, rapid, aimless muscle motor and / or vocal tic in one or more parts, and can be accompanied by hyperactivity, inattention, obsessive-compulsive movements and thinking or other behavioral symptoms. The long-term use of western medicine has extrapyramidal adverse reactions, such as drowsiness, nausea, etc., and cannot fundamentally prevent the occurrence of the disease, the need for long-term medication, but the persistence of medication in children is uncertain. Obvious rebound phenomenon can be produced after drug withdrawal, which makes it difficult for clinical treatment. Traditional Chinese medicine in the treatment of TD is the overall regulation of multiple neural energy systems, and traditional Chinese medicine can be combined with acupuncture, massage and other treatment methods for comprehensive intervention. In recent years, more and more clinical studies of traditional Chinese medicine have brought hope for the treatment of TD in children in the future. This paper summarizes the progress of clinical treatment of TD in children with traditional Chinese and western medicine, in order to provide new ideas and basis for the clinical treatment of TD in children.

1. Foreword

Children's tic disorder is a neurodevelopmental disorder that begins in childhood, which is characterized by muscle contraction, that is, involuntary, rapid, aimless muscle motor tic and / or vocal tic in one or more parts, and may be accompanied by hyperactivity, inattention, obsessive-compulsive movements and thinking or other behavioral symptoms [1]. In recent years, the incidence of tic disorder has increased year by year. According to epidemiological investigation, the total prevalence rate of TD in China is about 6.1% (1.7%), which is the most common type of TD in children, followed by CTD (1.2%) and TS (0.3%). And males are significantly more than females [2]. According to the clinical characteristics and course of the disease, DSM-5 divides TD into three types, including TS, chronic TD and transient TD [3] (see Table 1). Children with tic disorder tend to be complicated with attention deficit hyperactivity disorder, emotional disorder, and

the more co-diseases, the greater the adverse impact on children's life, learning and social interaction, so early detection is very important for timely treatment. The exact etiology and pathogenesis of tic disorder are unclear. Western medicine's treatment of tic disorder mainly includes psychotherapy, behavioral regulation therapy and western medicine treatment. Although western medicine can quickly relieve tic symptoms, the condition is easy to be repeated. Traditional Chinese medicine has achieved a certain effect in the treatment of TD, and there is no lack of reports on the treatment of integrated traditional Chinese and western medicine, so looking for a more effective comprehensive treatment is one of the key questions at present.

Table 1: Typing of tic disorder

Type	Symptom	Course of disease
TTD	To move or make a sound.	Less than 1 year
CTD	To move or make a sound.	More than 1 year
TS	To move and make a sound.	More than 1 year

2. Etiology and Pathogenesis of Western Medicine

At present, the etiology and pathogenesis of tic disorder are still unclear. Under the research of modern scholars, all kinds of pathogenesis hypotheses have been put forward for clinical reference. Western medicine believes that tic disorder in children is a neurodevelopmental disorder, and its pathogenesis may be the result of neurobiochemical, genetic, immune, psychological and environmental factors. At present, neurobiochemical factors are generally recognized as the cause of TD. The occurrence of tic symptoms is mostly considered to be related to the imbalance of neurotransmitters such as dopamine and 5-HT, resulting in the imbalance of executive attention loop, emotional loop, selective attention loop, impulse / compulsion loop and hyperactivity loop in the cortex-striatum-thalamus-cortex circuit. Clinical studies by Wang Xiaoyong and others have found that the total effective rate of haloperidol is 76.74%, indicating that the incidence of TD is closely related to DA receptors [4]. Most scholars believe that the incidence of TD is related to genetic factors, and there is a tendency of familial aggregation. A family study on TD found that the incidence of transient TD in the same family was 40-50% [5]. At present, no specific genes and genetic patterns have been found, and previous research results are difficult to be further replicated to confirm. Therefore, exploring the susceptibility genes and genetic patterns of TD is still an important content that needs to be studied. Some scholars also believe that the occurrence of TD is related to the abnormal immune response of the immune system to various pathogens infected by children, such as type a streptococcus [6]. Recurrent tonsillitis and upper respiratory tract infection are also easy to induce tic symptoms [7]. Zhu Xuemi [8] and other studies found that the levels of blood lead and blood zinc in serum are the risk factors for the pathogenesis of TD. The increase of blood lead and the decrease of blood zinc eventually lead to nerve endings dysplasia, which leads to abnormal information transmission. Mental and psychological stress of pregnant women, diseases (malnutrition, threatened abortion, etc.) and bad living habits (smoking, drinking, etc.) may affect fetal brain development, resulting in an increase in the prevalence of tic disorders in children [9]. In addition, perinatal infection, fetal asphyxia, amniotic fluid aspiration, premature delivery and overdue delivery are also easy to cause DNA methylation and increase the risk of tic. Poor growth environment can cause mental stress, such as tension, anxiety, fear and other emotions, which can cause or aggravate tic symptoms.

3. Western Medicine Treatment

3.1 Drug Treatment

3.1.1 Dopamine Receptor Blockers

It is the first drug used to treat tic disorder in children. However, due to its prominent adverse reactions, such as excessive sedation and prolonged QTc, it has been reduced from first-line drugs to patients with careful selection, severe involvement and other treatment resistance [10]. Tiapride is a benzamide selective dopamine antagonist, which can inhibit midbrain peripheral dopamine nerve hyperfunction, combat striatal dopamine nerve dysfunction, reduce tic symptoms by 76%, and have fewer adverse reactions [11]. Tiapride is a first-line drug recommended by European and domestic experts for the treatment of TD in children.

3.1.2 Dopamine Receptor Agonists

Aripiprazole, an atypical antipsychotic drug, reduces dopaminergic neurotransmission through D2 partial agonists. In addition, it is also a partial 5-HT1A agonist and 5-HT2A antagonist, which is as effective as tiapride, reducing tic by 60.2%, with mild side effects [12]. Yang Chunsong et al found that the adverse reaction rate of aripiprazole in the treatment of tic disorder in children was lower than that of tiapride, haloperidol, risperidone and other drugs [2]. Aripiprazole has become a common drug in the treatment of tic because of its good effect on tic and less prominent adverse reactions.

3.1.3 Selective Monoaminergic Receptor Antagonists

Risperidone, which acts through antagonism of dopamine D2 receptor and 5-HT2 receptor, is one of the best studied antipsychotics in the treatment of tic disorder [13]. However, its side effects are mainly weight gain and sedation, so its long-term efficacy and safety need to be further studied in children [14].

3.1.4 A-Adrenoceptor Agonist

Norepinephrine drugs are more commonly used in children and adolescents than in adults, mainly in patients with ADHD and mild tic [15]. Clonidine, a commonly used clinical α -adrenoceptor agonist, can be used as oral and transdermal preparations. Clonidine is mainly used to treat moderate tic children and adolescents in the treatment of tic disorders. Clonidine transdermal patch is more convenient and safe to use. Compared with traditional drugs for tic disorder, it has no significant difference in efficacy and has the advantages of less side effects. Guo Jingmin and other studies found that the clinical effect of haloperidol was slower than that of haloperidol in children with moderate and severe tic disorder. 3-4 weeks after the drug took effect, there was no significant difference between the two groups, and they had the advantage of less side effects [16]. Guanafaxine is another alpha-adrenoceptor agonist that reduces tic and improves ADHD symptoms in children and adolescents. The most common adverse reactions of guanafaxine are sedation, headache, fatigue, dizziness, irritability, epigastric pain and nausea, which usually occur within the first 2 weeks of administration and are usually relieved [17]. In particular, the sustained-release preparation of guanafaxine may induce QTc lengthening, so patients should be monitored accordingly.

3.1.5 Other Medicament

Extractive analysis showed that THC had no significant benefit in treating TS compared with placebo. No serious adverse reactions were reported, only mild adverse reactions, including dizziness, fatigue and dry mouth [18]. Topiramate is a kind of fructose diacetone modified by amino acid ester, and its mechanism is unknown. Some scholars believe that topiramate may reduce nerve excitability and improve abnormal behavior by reducing the release of excitatory amino acids in serum. Compared with haloperidol and tiapride, it has good efficacy and tolerance in patients with TS [19].

3.2 Non-Drug Therapy

3.2.1 Psychological and Behavioral Therapy

Psychological and behavioral therapy is the most commonly used adjuvant therapy for children with tic disorder in clinic. Through psychological counseling to children and parents, adjust their psychological state, eliminate the sense of shame, and adopt health education to guide children, parents and teachers to correctly understand the disease and play down the tic symptoms of children. Psychotherapy for mild children, drug therapy and psychotherapy for moderate and severe children, and individual treatment can promote psychosomatic rehabilitation [20].

3.2.2 Behavioral Intervention

Behavioral intervention plays a positive role in relieving tic symptoms of children with TD to some extent. The main thing is to guide the children through positive reinforcement, relaxation training, and negative practice and reverse behavior training to improve their bad behavior [21]. Giving children multi-sensory comprehensive stimulation in a specific environment can make the connection of children's brain nervous system more mature and effective, provide children with the ability to integrate complex information in the environment, promote children's adaptability and increase their self-confidence. It is helpful for children to communicate with parents and doctors.

3.2.3 Neuroregulation

Neuroregulatory therapy mainly includes repetitive transcranial magnetic stimulation, EEG biofeedback and transcranial microcurrent stimulation, which can improve the tic symptoms of children by intervening the neurophysiological process in the deep part of the brain. The study found that repeated transcranial stimulation of secondary motor areas (supplementary motor area, SMA) with frequency 1Hz, 100% intensity threshold, no adverse events were found, and tic symptoms were improved after treatment [22]. Many domestic researchers use EEG biofeedback to treat children with TD. By collecting EEG and EMG, real-time feedback is carried out with various images, mainly to improve SMR and reduce theta wave as the treatment plan. Many hospitals in China have applied this prescription to treat children with TD and achieved varying degrees of curative effect. DBS is an invasive treatment, which is only used in elderly children or refractory children, but has not been widely used in the treatment of other types of TD in children. It is speculated that it may be effective in the treatment of refractory TD in children.

3.2.4 Family Support Therapy

A relaxed and harmonious family atmosphere can reduce children's inferiority complex, reduce their psychological defense level, and relieve tic symptoms. Strengthen the psychological nursing guidance of parents, so that family members can correctly understand and treat the disease, actively

face and correctly guide the treatment of children, and play a positive role in the treatment of tic disorder of children.

4. Etiology and Pathogenesis of Traditional Chinese Medicine

With regard to the etiology and pathogenesis of TD in traditional Chinese medicine, there is no clear name of tic disorder in traditional Chinese medicine, but there are many related records in ancient books, which are classified as "liver wind", "chronic infantile convulsion", "tic" and so on. Most doctors argue that "liver wind" is the main pathogenesis of the disease according to the clinical manifestations such as eyes, corners of mouth and limb twitch, and think that "domination of wind-evil may disturb the body" is the main pathogenesis of the disease. The location of the disease is mainly in the liver, involving the heart, spleen, lung and kidney. The pathological factors are wind, fire and phlegm. The causes are mainly caused by birth injury, lack of congenital endowment, improper diet, emotional imbalance, external evil invasion and so on. According to its key pathogenesis, traditional Chinese medicine puts forward the main treatment principles of suppressing hyperactive liver for calming endogenous wind, and dialectically treats them according to the individual condition of the children and the different syndrome types and deficiency and excess of the disease.

4.1 Traditional Chinese Medicine Treatment

In recent years, the clinical research and basic research on the safety and efficacy of traditional Chinese medicine in the treatment of various syndrome types of TD have been deepened. In view of the wind evil invading the lung type TD, Professor Ma Rong [23] believes that "the external wind can induce the internal wind", and the attack of the wind evil causes stagnation of the qi and obstruction of the meridians, which is caused by multiple muscle wind convulsions. Therefore, the prescription selects Yinqiao powder to add and subtract, to evacuate wind and heat, clear the lungs and calm the liver, treat both internal and external wind, and stop when the wind goes out. Xu Jingyun [24] divided 108 patients with wind-induced TD with liver hyperactivity into Tiapride group and Tianma Gouteng decoction plus or minus group. The results showed that the scores of main and secondary symptoms of TCM in both groups decreased after treatment, but the total effective rate and total incidence of adverse reactions in Tianma Gouteng decoction group were better than those in tiapride group. Wang Qing [25] used modified Huanglian Wendan decoction to treat children with TD syndrome of phlegm-heat and wind. It was found that the level of mi-Rmur429 in peripheral blood of children with tic disorder was significantly increased, and the scores of YDTSS and TCM syndromes were also significantly decreased. Cui Liping et al [26] divided 54 children with Tourette syndrome into Qinggan Dayu decoction combined with acupuncture treatment group and Tiapride treatment group. After 2 months of treatment, the results showed that traditional Chinese medicine plus acupuncture could regulate the balance of yin and yang in children with Tourette syndrome. The tic symptoms were significantly improved, and compared with Tiapride, the recurrence rate was lower and the safety was higher. In clinical treatment, the compound prescription of traditional Chinese medicine has the advantages of definite curative effect, minor adverse reactions and concomitant symptoms. The continuous deepening of clinical research on traditional Chinese medicine compound prescription brings hope for the treatment of TD in children in the future.

4.2 Treatment of Proprietary Chinese Medicine

In clinic, Changma Xifeng tablet is often used to treat the syndrome of hyperactivity of liver with

phlegm in children with tic syndrome; Jiuwei Xifeng granule is used to treat children with Tourette syndrome of wind movement due to yin deficiency; and Shaomazhi granule is used to treat tic disorder of hyperactivity of liver and internal disturbance of phlegm and fire. In a multicenter, randomized, double-blind, double-blind, positive drug-controlled trial conducted by Ma Rong [27], 438 patients with tic disorder were randomly assigned to receive Tiapride tablets or Changmaxifeng tablets. The results showed that the clinical effect of Changma Xifeng tablet in reducing tic was not inferior to that of Tiapride, and the incidence of adverse reactions was less than that of Tiapride. In a multicenter, double-blind, randomized, placebo-controlled clinical study conducted by du Chunyan and Hu Siyuan [28], 144 children with tic disorder were randomly divided into two groups: Jiuwei Xifeng granule group and placebo group. And Jiuwei Xifeng granule is safe in the treatment of tic disorder in children. Han Xinmin [29] in a multicenter, double-blind, double-simulated, randomized, placebo-controlled trial, 603 children with TS aged 5-18 years old were randomly assigned to receive placebo (n = 117), tiapride (n = 123, 200-400 mg/d) or Wuling granule (n = 363, 15.0-22.5 g / d). The results of continuous observation for 8 weeks showed that the clinical efficacy of Wuling granule in reducing tic was comparable to that of tiapride. But its safety is better than that of sulphiride.

4.3 Acupuncture Treatment

Acupuncture is the most commonly used technical operation in traditional Chinese medicine, the use of different acupuncture or moxibustion techniques to stimulate certain acupoints on the human body, through meridians and acupoints, adjust human viscera qi and blood, to achieve the purpose of treating diseases, it plays a positive role in the treatment of tic disorders in children. Ye Donglan [30] took Taichong, Sanyinjiao, Hegu, Shenmen, Baihui, Sishen Cong, Fengchi and Lianquan, and then treated 82 cases of tic disorder with flat tonifying and purging acupuncture after gently twisting qi. The course of treatment was 21 days. The results showed that the effective rate of treatment was 91.5%. No obvious side effects were found in the follow-up within half a year. Wu Huifen et al [31] were treated with auricular point pressing in 16 cases, and followed up for 3 months, the total effective rate was 87.5%. In a randomized controlled study of Dai Weifeng and Han Xue [32], the control group was treated with Zishen Pinggan recipe, while the treatment group was treated with acupuncture combined with auricular point sticking on the basis of the control group. After continuous treatment for 2 months, the levels of DA and 5-HT in the two groups were significantly lower than those in the same group before treatment, while the levels of GABA in the treatment group were significantly higher than those in the same group.

4.4 Massage Therapy

Massage is based on the basic theory of traditional Chinese medicine, to push, take, point, press, and kneads and other techniques to act on the corresponding parts, stimulate the corresponding acupoints or meridians, in order to treat diseases. The main hand methods for the treatment of children's tic disorders are pushing and kneading the spleen soil, pounding the small Tianxin, kneading the five fingers, transporting the gossip, dividing yin and yang, pushing up the three passes, rubbing Yongquan and Zusanli. Shen Hongyan et al [33] randomly divided 70 children with TD of wind-moving and phlegm type of liver hyperactivity into observation group (n = 35) and control group (n = 35). The observation group was treated with Wenjing decoction combined with Anshen Ningzhi massage (mainly scalp and facial acupoints, Baihui, Sishencong, sun, Cangzhu, etc.), while the control group was treated with the above-mentioned traditional Chinese medicine. Results the cured and markedly effective rate in the observation group was significantly higher than that in the control group. Lin Xiaohong [34] summed up Professor Luo Xiaohong's experience in

treating TD from the liver and spleen. Sini San combined with Sijunzi and Wendan decoction was used in traditional Chinese medicine, and on this basis, combined with tonifying the spleen meridian, clearing the liver meridian, tonifying the kidney meridian, head four methods, etc., the curative effect was remarkable.

5. Summary

With the in-depth study of TD in children, more and more treatments have emerged and achieved phased results. TD is a complex multi-factor disease, and the curative effect of a single treatment is not good, so it needs to be intervened by the combination of Chinese and western medicine. In the treatment process of integrated traditional Chinese and western medicine, the corresponding treatment methods should be selected according to the clinical type and severity. For example, children with transient tic disorder or mild children are mainly treated with cardiology and traditional Chinese medicine; for children with chronic motor or vocal tic disorder, vocal and multiple exercise combined tic disorder or moderate and severe tic disorder, they are mainly treated by combination of traditional Chinese and western medicine, combined with psychotherapy. Holding and so on also has a certain effect on tic disorder. The treatment of integrated traditional Chinese and western medicine can promote their respective strengths, avoid their weaknesses and improve their curative effect.

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