Brief Discussion on the Research Progress of Sanbia Decoction in the Treatment of Migraine

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Abstract: Migraine is widely regarded as a frequent symptom of chronic brain dysfunction, and its persistent and periodic attacks may lead to serious health problems, a decline in quality of life, and a decrease in work efficiency. At present, it has become one of the most concerned issues in the global public health field. Western medicine treatment of migraine has shortcomings, such as difficult to treat the root causes, large side effects, easy drug reliance, and a single treatment method of treatment, so traditional Chinese medicine has shown great potential and prospects. Sanbia Decoction is included in Chen Shihou’s Dialectical Record of the Qing Dynasty. Its effect is to relieve wind and relieve pain, and benefit Modern pharmaceutical studies show that Sanbia Decoction achieves the purpose of regulating inflammatory factors, analgesic, maintaining vascular homeogenesis, regulating immune function and hormone levels by regulating the levels of calcitonin gene-associated peptide (CGRP), strychnotropin (5-HT), tumor necrosis factor-α (TNF-α), ni This study summarizes the mechanism of Sanbia Decoction in treating migraines, the clinical observation of Sanbia Decoction, the experience of famous traditional Chinese medicine prescriptions, and points out some existing problems to provide relevant reference for the majority of medical researchers.

Keywords: Sanbia Decoction, Migraine, Analgesia, Review.

1. Introduction

Migraine is a primary headache characterized by paroxysmal unilateral or bilateral middle or severe pulsating pain. It is often accompanied by symptoms such as nausea, vomiting, photophobia, phophobia and other symptoms, which generally lasts for 4 to 72 hours. Migraine is a chronic neurovascular disease with the characteristics of repeated attacks. In China, the ratio of men to women with migraine is 1:2 to 3, and the prevalence rate is 5% to 10%. The GBD study shows that the number of people diagnosed with migraine is increasing year by year, which is one of the diseases that affect the health of our people [1]. Migraine is closely related to anxiety, depression, insomnia, history of cardiovascular and cerebrovascular diseases, and emotions [2]. However, the pathogenesis is still unclear. At present, the theory of trigeminal neurovascular disorder and the theory of cortical diffusion inhibition (CSD) are highly recognized. Migraine is often divided into four stages: prodromal stage, precursor stage, headache period and recovery period. The mild unsuitable symptoms in the prodromal stage, such as loss of appetite, stiff neck, etc., are often ignored by patients. Abnormal visual, sensory and verbal symptoms can occur during the precursor period, and visual precursors are the most common. During the headache period, 60% is unilateral pain and 40% is bilateral pain, characterized by pulsating pain. Recovering patients can relieve themselves after 4-72 hours of attack [3]. At present, there are acute non-specific drugs for migraine: non-steroidal anti-inflammatory drugs (NSAIDs) (bufrofen, sodium diclofenac, aspirin, nappision) p-acetaminophen, containing caffeine compound preparations; specific drugs: trabutam: (Shumaputam, Lizartrabutam, Zomitrabutam), ergotamines (5-HT1B/1D receptor agonists), ditan drugs (lamidetamidetan), and gipan drugs (remejipam) [4].

In the long history of traditional Chinese medicine, the research and treatment of headaches have been recorded in detail. Headaches usually belong to the categories of diseases mentioned in ancient books, such as "head stroke", "jue headache", "brain wind", "shoufeng" and "true headache". These diseases are often caused by visceral dysfunction caused by external evil attacks or internal injury miscellaneous diseases, or trauma. The name "headache" is proposed for the first time in the Yin and Yang Shihui Mai Jiu Jing. The earliest record of headache can be traced back to the Huang Emperor's Neijing: "A new stroke is the first stroke, ... is a brain wind". In the SuWen-Fang Sheng Shuai Lun, it is also mentioned that "the situation of qi does not fall, the top of the headache" is also mentioned. The syndrome differentiation and treatment of headache are described in detail in the Theory of Typhoid Fever, including the use of the Six Jing Differentiation Syndrome to divide different types of headaches, such as "Jiuyin headache, or spitting, Jueheng, its pulse is floating and slow, Wu Zhuyu Decoction". The "Jianxi Xin Fa" emphasizes the importance of phleghm and fire in the onset of headaches, and provides drug treatment plans for headaches in different parts, such as "Sun Headache can use Chuannxiang. Yangming Headache can use Baizhi. Shaoyang Headache can use Chaihu. Taiyin Headache can useAtractyshu. Shaoyin Headache and Jueyin Headache can use Wu Zhuyu". "Jisheng Prescription• Treatment of Headache" further elaborates the characteristics of Jue headache: "Everyone with headache, deficiency of qi and blood, the evil of wind, cold, heat and dampness, injury to the yang meridian, and those who can't stay, and are called Jue headache". "Medical Guide • Headache" records the use of different treatment methods and traditional Chinese medicine for different syndrome types of headaches. Jingyue Quanshu points out that "all those who diagnose headaches must have both vitality". "Lenglu Medical Words • Headache" further explains the characteristics of different types of headaches: "Sun headache reaches the top of the top. Yangming headache forehead pain. Shaoyang headache pain on both sides of the temples. Jueyin headache will be on the top". Wang Qing is
2. Composition and Efficacy of Loose Soup

Sanbia Decoction is included in Chen Shiduo's Dialectical Record of the Qing Dynasty. Its effect is to relieve wind and relieve pain, and benefit liver and gallbladder. It is a common prescription for the treatment of migraines. Clinically, it is often added or subtracted, and it is good at treating migraines of liver and gallbladder depression and wind attacking Shaoyang. Loose soup consists of five cents of white peony, one tael of Chuanxiong, one coin of Yu Liren, one coin of Chaihu, three cents of white mustard, two cents of fragrant attached, one coin of liquorice and five cents of angelica. Modern metering can be converted to: 15g white peony, 30g of Chuanxiong, 3g of Yu Liren, 3g of Chaihu, 9g of white mustard, 6g of fragrance, 3g of liquorice, 1.5g of Angelica [5]. Chuanxiong tastes Xinsan, the upstream leader, downstream blood sea. Zhongkai Yujie, is the Qi medicine in the blood, and the main medicine. White peony nourishes blood and softens the liver, restrains yin and relieves sweating. The combination of liver and yang and liquorice can not only slow down and relieve pain, but also prevent the Xinlie of Chuanxiong; Chaihu and Xiangfu soothe the liver, recuperate Qi machine, Angelica dahuurica to relieve the surface and dispel cold, dispel wind and relieve pain. Chaihu and Angelica dahuurica are also citation drugs for Shao yang and Yangming headaches, which can make the effect of the drug directly reach the lesion. White mustard, open phlegm and promote qi, clear collateral to relieve pain, and search for wind phlegm inside and outside the skin. For medicine. Yu Liren, the main drop of medicinal properties, prevents the king's medicine Chuanxiongxin from dispersing too much, and has the effect of lifting the cause, as a supporting medicine. Licorice blends medicinal properties, and relieves pain as medicine. Only when all the medicines are compatible can they achieve the effect of "the general principles are painless". Modern pharmacological studies have shown that Chuanxiong has the effects of analgesic, anti-oxidation and protection of brain nerves [6]. The active components in Chuanxiong include Myricanine, which acts on key targets such as PTGS2 and MAPK14, and participates in the regulation of the vascular process of the circulatory system and the regulation of vascular diameter of the body. At the same time, they also participate in the signaling pathways for the treatment of migraines, such as PI3K-Akt signaling pathway and estrogen signaling pathways [7], thus alleviating vasospasm. The use of Chuanxii and Bai Shao can relieve migraine symptoms by inhibiting pain sensitivity and improving the pain threshold and mechanical pain threshold [8]. The saponins of chaihu has a significant anti-inflammatory effect and can inhibit the expression of induced nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), thus reducing the synthesis of NO and prostaglandin E2 (PGE2) [9], Bai Zhixiang comarin and Bai Zhi volatile oil in Bai Zhi restore the balance of vascular active substances by reducing the levels of CGRP, NO and endothelin (ET) in the blood, thus reducing the further damage of blood vessels and nerves, relieving neurogenic inflammation, and playing a preventive role in migraine [10]. Xiangfu volatile oil in Xiangfu has antioxidant, anti-inflammatory, anti-allergic, antibacterial, analgesic and other effects [11], so it has a certain curative effect on migraine. White mustard and mustarin in white mustard have anti-inflammatory and analgesic effects [12-13], which is effective for early inflammatory reactions and pain symptoms of migraine. The combined use of peony and licorice has an analgesic effect and can effectively reduce the levels of inflammatory factors PGE2 and NO. At the same time, it can also improve the level of anti-inflammatory factors IL-10 [14].

3. Study on the Pharmacological Mechanism of Sanbia Decoction in the Treatment of Migraine

3.1 Regulate Inflammatory Factors

Inflammation is an early reaction of migraine. Among them, the trigeminal neurovascular theory believes that the neurogenic inflammation of migraine is importantly related to CGRP, 5-HT, TNF-α, etc. [15]. In the early stage of migraine, 5-HT is released in large quantities by platelets, causing cerebral blood vessels to contract, increase permeability, and reduce blood flow, thus causing vascular inflammatory reactions [16]. CGRP plays a role in dilating cerebral blood vessels, promoting inflammatory response, increasing nerve sensitivity and enhancing pain in the pathogenesis of migraine [17]. CGRP can participate in inflammatory reactions by activating mast cells to release histamine [18]. TNF-α stimulates the hypothalamus to produce inflammatory factors, activates platelets to release 5-HT, etc., further aggravating the inflammatory reaction [19].

Wang Kun et al. [20] Animal studies have shown that Sanbian decoction has a good effect on neurogenic inflammation of migraine, and its mechanism of action is mainly achieved by blocking the p38 MAPK/iNOS pathway. This mechanism helps to reduce the activity of inflammatory promoters such as NO, TNF-α, interferon γ (IFN-γ) and interleukin 1β (IL-1β), thus reducing the response to neuroinflammation. [21] Animal studies such as Liu Yan showed that decoction played a role in reducing the release of CGRP by the trigeminal nervous system. This mechanism of reducing CGRP levels can help curb the neuroinflammatory response caused by CGRP. At the same time, Sanbia decoction can also prevent CGRP from stimulating the degradation of mast cells and reduce the release of inflammatory media such as histamine, TNF, 5-HT and IL, thus effectively relieve migraine symptoms. Li Minmin et al. [22] Sanbiantang intervened migraines by manipulating two key ways: IL-17 and NF-kB. Blocking the NF-kB pathway effectively reduces the inflammatory activity around the cerebral blood vessels. At the same time, it can also reduce the release of various inflammatory factors by inhibiting the activity of the IL-17 pathway, thus helping to reduce inflammatory reactions and provide support for the treatment of migraines.

3.2 Analgesia

Pain is one of the main symptoms of migraine. Migraine is mainly attributed to the imbalance between the endogenous analgesic mechanism of the trigeminal nervous system and the central nervous system. When the end of the trigeminal
nerve receives external stimulation, it releases chemicals such as neuropeptides (SP), CGRP and NK, which in turn triggers blood vessel dilation and increases the sensitivity of the trigeminal nerve. These stimulation signals are transmitted to the island obo and frontal buckle cortex of the brain through the trigeminal nerve and its secondary and tertiary neurons, causing a headache. In the process of regulation, 5-HT, as a key neurotransmitter, regulates the secondary neuron function of the trigeminal nerve in the endogenous analgesic system [23].

Huang Lin and other [23] animal experiments showed that the effect of Jiawei Sanbian decoction in the treatment of migraine was more significant than that of the western medicine Shumaputan. And it also showed obvious analgesic effect. The mechanism is to reduce the content of chemicals such as SP, CGRP and NK in the blood. Liu Yan et al. [24-25] research shows that Sanbian decoction can effectively improve the symptoms of migraine model rats induced by nitroglycerin. Sanbian decoction blocks the pain signal transmission of the trigeminal nerve by inhibiting the calcium ion flow process activated with CGRP and NO, thus enhancing the analgesic effect of the endorphin system. Specifically, Sanbia decoction can reduce the activity of CGRP in the middle brain and trigeminal ganglion, and at the same time improve the expression level of the analgesic substance pre-endorphin (PENK) in these areas. [26] Clinical studies such as Wang Yongli show that Sanbia Decoction (Chuanxiong 30g) achieves vasodilation and enhances platelet aggregation by reducing the regulation of PGE2 and 6-ketone-prostaglandin F1α (6-PGF1α) in serum and raising the level of thromboxane B2 (TXB2). This regulation can not only prevent the activation of the meningeal pain receptor, but also reduce pain allergies, thus effectively alleviating the symptoms of migraine.

3.3 Maintain Vascular Homeostasis

Relevant researchers, by comparing the whole genome sequences of migraine patients with healthy people, and founding a new type of migraine susceptibility gene locus related to blood vessels and smooth muscle tissue, which highlights the key role of endothelial function in migraine attacks [27]. The cause of migraine is the disorder of the contraction and expansion function of blood vessels, the damage of vascular endothelial cells and the weakening of function [28]. Vascular active substances, such as ET-1 and NO, have a significant impact on migraine attacks. They have an effect on blood vessels in the brain, causing abnormal contraction of cerebral blood vessels, thus causing headaches [29].

The active ingredients of Sanbiano decoction are percuscin, rhinoside, and saponin [30]. Quinacrin, a flavonoid compound, whose effects include anti-inflammatory, antioxidant, restoring cerebral vascular function damaged by ischemia, and regulating the proliferation of vascular cells [31]. EPCs can differentiate into vascular endothelial cells and have the function of promoting the regeneration of blood vessels and repairing damage. The oxidative stress response of migraine will affect the proliferation, differentiation, adhesion and migration functions of EPCs [32]. Sun Jun et al. [33] studies have shown that the proliferation ability of EPCs cells can be enhanced through quercetin, and then the Akt protein inside EPCs and its phosphorylation forms rise. At the same time, it also improves the RNA levels of PI3K and Akt3m, thus inferring that quercetin may protect EPC's cells by activating the PI3K/Akt signal pathway. Therefore, the quercetin in Sanbian soup plays a certain role in maintaining the vascular homeostasis of migraine.

In vascular endothelial cells, endogenous endothelin-1 (ET-1) is the main factor that promotes vasoconstriction, while NO is the factor that promotes vasodilation. When the balance between ET-1 and NO is broken, it may lead to disorders in the contraction and diastolic function of blood vessels, causing headaches [34]. Feng Miao et al. [34] Research showed that the expression of 5-HT in serum in the treatment of 100 patients with migraine decoction was significantly higher than that in the control group. At the same time, the expression of ET-1 showed a significant downward trend in the experimental group. This shows that Sanbia decoction can reduce 5-HT in serum, weaken vasoconstriction, and reduce the onset of migraine. Zhang Guoni and others [36] showed that among the 88 patients treated, Xiongchong Sanbia Decoction observed a decrease in the content of ET-1 in the treatment group, while the content of NO increased. At the same time, the levels of inflammatory factors such as IL-6 and TNF-α also show a downward trend, while 5-HT levels have increased. In addition, the patient's migraine pain score, frequency and duration have been reduced. The blood flow rate of cerebrovascular vessels has also been significantly improved. It can be seen that Xiongchong Sanbia Decoction can effectively reduce the ET-1 level and improve the NO level, improve vascular symptoms, and prevent migraine.

3.4 Regulate Immune Function and Hormone Levels

Although the pathogenesis of migraines are unclear, they are closely related to immunity [37]. After the attack of cortical diffuse inhibition (CSD) of migraines, the activity of key genes increased, leading immune cells to strengthen protein synthesis. This causes the activation of inflammatory reactions, which in turn plays an important role in the occurrence, persistence and spread of migraine pain [38]. Relevant research articles also show that in the case of migraine, the function of Treg cells (regulatory T cells) has changed, and the amount of anti-inflammatory factor transformation growth factor-β (TGF-β) produced by them has decreased, resulting in a weakening ability to suppress neurogenic inflammation caused by inflammatory factor IL-17. This situation further exacerbates the imbalance of the immune system, thus increasing the frequency of migraine attacks [39]. Guo Honglei et al. [30] Network pharmacological studies have shown that the active ingredients in Sanbian decoction, quercin, rhinoside, and annaphol make the signal pathway of the IL-17 family play a key role in the immune response. When these signals are activated through the corresponding receptors, they promote the increase of the expression of downstream pathways, such as NF-κB, MAPKs and chemokines, activate T cells, and thus promote the release of inflammatory cytokines. The IL-17 family plays an important role in inducing and regulating the body's multiple immune responses. They play a vital role in protecting the host and regulating acute and chronic inflammatory reactions.
Estrogen can cause migraines by influencing mediated neurotransmitters, vascular endogenous contractile factors, substance P and regulating the endogenous opioid peptide receptor system [40]. One of the pathways that can treat migraines is the estrogen pathway [22]. Experiments such as Jing Xiaju and others [41] show that estrogen is positively correlated with the NO level in the serum of rats, which can reduce the level of ET-1 in the blood of ovary rats, thus relieving migraine. The mechanism is that migraine belongs to vascular headache. When the balance between ET-1 and NO is broken, it may lead to vascular There are disorders in contraction and diastolic function, which leads to migraine. Fan Hongzhen And Other Studies [42] showed that estrogen occurs with the activation of oxidative stress in migraines, and it is possible to activate the Nrf2/ARE signaling pathway, so that cell protection proteins cannot remove free radicals, reduct peroxides, and cannot combat oxidative stress, and affect chronic migraines.

4. Clinical Application of Sanbia Decoction

4.1 Clinical Observation of Sanbia Decoction

Guo Xiajun and others [43] clinical observation showed that for 60 patients with clinical liver qi stagnation, the clinical effect experimental group of Sanbia Decoction combined with Kaisiguan was better than the nourishing serum brain pills taken in the control group, and the VAS score of the experimental group was lower than that of the control group, indicating that the combination of Sanbia decoction combined with Kaisiguan was significant in the treatment of migraine and had a role in alleviating pain. Clinical observation of Yifeng et al. [44] showed that for 88 migraine patients, the content of 5-HT and calcitonin gene-related peptides in the experimental group was much lower than that of the control group that simply took flunarizine hydrochloride, and the recurrence rate of headache was lower than that of the control group and the safety of the control group was higher than that of the control group. Clinical observation of Wang Zhao et al. [45] showed that for 72 cases of vestibular migraine, Sanbian decoction combined with flunarizine hydrochloride was significantly improved compared with the number of attacks, dizziness time, anxiety and depression after the control group, indicating that Sanbian decoction and flunarizine hydrochloride effectively treated migraine and depression and anxiety in patients. It plays an improvement role. Clinical observations of Ren Dongdong and others [46] show that for 46 patients with wind phlegm and blood stasis migraine, after treatment with Jiaweisian decoction, the level of CGRP and ET in the patient's plasma is reduced, and the number of painkillers is reduced, indicating that Jiaweisian decoction can relieve pain by reducing the level of CGRP and ET in plasma. Resolve migraines. Clinical observation of Gu Hongyu and others [47] showed that for 108 migraine patients, the control group was treated with flunarizine hydrochloride, and the experimental group was treated with acupuncture. Four weeks after treatment, the average water of 5-HT, CGRP and DA in the experimental group was higher than that of the control group, and the average water of ET-1 and NO was lower than that of the control group. It has been proved that compared with simple Western medicine treatment, traditional Chinese medicine has more advantages to improve the frequency, duration and degree of headache attacks.

4.2 Application Experience of Old Chinese Medicine

Professor Ge Jinwen [48] In actual clinical treatment, Professor Ge found that the combination of Sanbian soup and Xuanqi soup has a significant effect. This combination covers the treatment of the three meridians of traditional Chinese medicine: the Sun Meridian, Yangming Meridian and Shaoyang Meridian. The prescription mainly contains wind-repelling drugs, which can also overcome dampness and remove blood stasis. In the treatment of migraine, this combined scheme shows good clinical results. Professor Lei Genping [49] In the actual clinical treatment, he made good use of ephedra fine fuji decoction to treat migraine. Clinically, Professor Lei stressed that when applying Santan decoction for clinical treatment, special attention should be paid to two key points. First of all, a higher dose of Chuaxiong must be used. Secondly, we should carefully grasp the ratio between Chuaxiong and Baizhi. In practice, Professor Lei tends to change the ratio of 30 grams of the original Zhongchuanxiong to 1.5 grams of Baizhi to a 20: 1 ratio to achieve the best effect. The famous doctor Qin Haoyue [50] made innovative adjustments to the traditional powder decoction in the treatment of female migraines. She removed the "Chaihu" and "Fragrant Attachment" with boiling and dry characteristics in the original prescription, as well as the moisturizing ingredients "Yu Liren", and chose medicinal herbs such as "Cang Erzi", "White Zombie Silkworm", "Tai Poria" and "Danshen". These medicinal herbs aim to dredge meridians more gently and dissipate head pain. At the same time, according to the unique physiological and migraine pathological characteristics of women, they are comprehensively treated from three aspects: wind, phlegm and blood stasis. This tailored powder decoction scheme shows a good therapeutic effect in practice. Professor Dai Ximeng [51] pointed out in the treatment of Migraine: the focus on the use of Chuaxiong, with a maximum dosage of 30 grams, especially for its characteristics of dredge meridians, blood circulation, qi, and relieve wind and pain, especially for headache; for severe pain, increase the dosage of white peony to 30 grams for its.

4.3 Integration with Academic Thinking

Li Yan [52] Through the theory of "long-term disease into the collaterals" and "long-term pain into the collaterals" proposed by Ye Tianshi, a member of the School of ferbidity, Li Yan [52], the creation of Tongluo Sanbian-bian soup: 10g each of stiff silkworm and Baizhi, 5g of dew beebee, 10g of red peony, 15g of Chuaxiong, 10g of Dilong, white mustard and Latong, and 3g of licorice. There are different additions and subtractions for various types of certificats: qi deficiency plus astragalus 30g, attractylodes 10g, liver fire plus ochre 20g, hook rattan 15g, scutella 10g Yin deficiency plus Shouwu 10g, ripe Dihuang 15g, wolfberries 10g, blood stasis plus ghost arrow feather 15g, Sanling and Liu Jinu 10g each. Phlegm plus Nanxing, Fabanxia, Huaju red 10g each. In contrast with flunarizine hydrochloride in the treatment of migraine, for four consecutive weeks, it is concluded that the effective rate of applying Tongluo Sanbian decoction is higher than that of the group using flunarizine hydrochloride. The NRS digital score, headache points, and frequency of painkillers are significantly lower than that of the flunarizine hydrochloride group. It can be seen that the theory of "long-term disease"
and "long-term pain" in combination with fever has obvious effect on the treatment of migraine.

Li Xin [53] Through the combination of Sanbia Decoction with the "Xuan Wei Fu" proposed by Liu Wansu in the "Suwen Xuanji Yuan Bing Shi"; it is proposed to match Tongli Xuanfu and Kaijie Sanyu stasis on the basis of Sanbia Decoction, and treat migraines according to the addition and subtraction of clinical symptoms. It consists of 30g of Chuanxiong, 15g of Tianma, Poria and Tulips, 20g fragrant attachment, 6g each of white peony, whole scorpion, and 12g of Chaihu. For those with cold coagulation and blood stasis, add 3g of dried ginger and Wu Zhuyu with Wu Qihai, Guanyuan, Shenque and other acupuncture points. Liver qi stagnation is matched with Taichong and between lines. The external feeling of wind and cold is matched with ephedra, Guizhi, Pu'eraria root with Fengfu, and it is missing. Qi and blood deficiency are matched with Angelica, cooked land, atractylodes and other qi and blood-replenishing drugs are matched with Xue Hai, Zusanli and Guanyuan. Phlegm turbidity and collaterals are matched with Banxia, Atractylodes and other antiphlegm and collaterals. Starting from the combination of three drugs: treating wind, clearing collaterals, and regulating qi and blood, Tongli Xuanfu, smooth veins and closure, and then migraines can be solved.

5. Summary and Outlook

As a traditional Chinese medicine prescription, Sanbia Decoction shows its potential and prospect in the treatment of migraine. With the in-depth study of traditional Chinese medicine in modern medicine, the efficacy and mechanism of Sanbia decoction have gradually been scientifically verified. In the future, the application of Sanbia Decoction may be more widely promoted, especially for migraine patients who seek alternative and complementary treatments. At present, research on the ingredients of Sanbia decoction has revealed its possible anti-inflammatory, analgesic and neuroregulating effects, which provides a theoretical basis for its treatment of migraine. Future research may focus on further clarifying its mechanism of action, optimizing drug ratios, and evaluating the safety and effectiveness of long-term use. At the same time, with the development of personalized medical treatment, Sanbian soup may be adjusted according to the patient's specific physique and condition to achieve better treatment effect.

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