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ORIGINAL ARTICLE

Effect of Cynomorium total flavone on depression model of perimenopausal rat

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KEYWORDS

Cynomorium total flavone;
Perimenopausal syndrome with depression;
Estradiol;
Estrogen receptor

Abstract *Purpose:* To observe the effect of cynomorium total flavone on the depression model of perimenopausal rat and to analyze the action characteristics of cynomorium total flavone on depression of rat with perimenopausal syndrome.

Method: Duplicate the model of rat with perimenopausal depression based on the combined method of incomplete castration and chronic stimulation, and keep drug administration for 35d. And then measure related behavior indicators and the change of biochemical index level in serum and brains; measure the estrogen/androgen receptor (ER/AR) in related tissues and the ERmRNA expression in hypothalamus.

Result: It can be seen that cynomorium total flavone can significantly improve the behavior indicators of rat with perimenopausal depression; obviously or significantly change the level of related biomedical indexes in serum and brains of perimenopausal depressed rat; obviously or significantly increase the expression of ER/AR in related tissues of perimenopausal depressed rat; obviously or significantly increase the ERmRNA expression in hypothalamus.

Conclusion: Cynomorium total flavone can adjust hypothalamic-pituitary-gonadal axis by increasing E2, and make related biomedical indexes and hormone receptors tend to be normal, so as to relieve perimenopausal syndrome and perimenopausal syndrome with depression.

1. Introduction

With the increase in age and decline of ovarian function, estrogen secretion is gradually decreased, which leads to the dysequilibrium of HPO and hypothalamic-hypophyscal-ovarian axis (HPOA) and impacts autonomic center function and the functions of various organs controlled by autonomic center, thus causing a series of symptoms called perimenopause syndrome (PMS) or climacteric syndrome (CS). Epidemiological investigation was performed for women's perimenopausal syndrome in Shanghai, showing that those with depression tendency account for 77.29% of total respondents, while those with depression symptoms account for 8.36%, and both belong to common symptoms of patients with PMS. Studies believe that the incidence of risk in general as early as 40 years old will begin to appear (Judy, 2011). In addition, studies have

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indicated that PMS symptoms can decrease the quality of life of PMS patients and increase the risk of the disease. So seeking another safe and effective therapy is in urgent need. At the initial phase of this experiment, we have done pharmacodynamic study on total flavonoids applied in mouse model of perimenopause. The study proves that total flavonoids from Cynomorium songaricum can improve related indicators of mouse model of perimenopause; but it lacks the discussion about the action and mechanism of total flavonoids from Cynomorium songaricum on animal models of perimenopausal depression. Therefore, this article will mainly study the action and mechanism of Cynomorium songaricum on the mouse model of perimenopausal depression.

2. Materials and methods

2.1. Experimental animal

SD rat; female; SPF level body weight: 250–270 g; Supplier: Shandong Lukang Pharmaceutical Co., Ltd.; Certification number of the animal: 0021925; Certification number of the laboratory: SYXK (Henan Province) 2010-001.

2.2. Experimental drug

Cynomorium total flavone prepared in Office of Chemistry, Henan University of Traditional Chinese Medicine, purity: 50.87%, batch number ZL20140716. Gengnianan capsules: produced by Shanxi Tianxing Pharmaceutical Co., Ltd. Batch number: 140112. Soybean Isoflavones Vitamin E Soft Capsules: produced by Weihai Purple Light Biotechnology Development Co., Ltd. Batch number: 14040301.

2.3. Experiment method

From 100 female wistar rats with weight ranging from 250 to 270 g, randomly selecting out 12 as blank group for sham-operation, and the menopausal models of the remaining rats are established. After weighing, injecting 10% chloral hydrate (0.3 ml/100 g) for anesthesia before fixing their abdominal regions, and then completely extirpating the left ovary and extirpating 80% of right ovary before suturing well the muscle and skin. After operation, carefully feeding them and injecting penicillin 200,000 u/kg (0.1 ml per rat) one a day for consecutively 3 days. From the 5th after operation, vaginal smear examination is applied on every single rat once a day for consecutively 5d. Those showing emotional reactions are not used, and finally 72 completely castrated rats are randomly divided into 6 groups including Gengnianan capsule group (fed with Gengnianan capsule suspension of 0.45 mg/kg, which equals 10 times of the clinical dosage), Soybean Isoflavones Vitamin E Soft Capsules group (fed with Soybean Isoflavones suspension of 0.167 mg/kg, which equals 10 times of the clinical dosage), big dosage cynomorium total flavone group (fed with 0.2 g/kg cynomorium total flavone, which equals 20 times of the clinical dosage), medium dosage cynomorium total flavone group (fed with 0.1 g/kg cynomorium total flavone, which equals 10 times of the clinical dosage), and small dosage cynomorium total flavone group (fed with 0.05 g/kg cynomorium total flavone, which equals 5 times of the clinical dosage). In addition, both blank group and model group are fed with 0.5% CMC solution of the same volume. Drug administration is given by 1 ml/100 g once a day for consecutively 35 days.

After keeping drug administration for 5 days, rats in the blank group are kept by 6 rats per cage without any simulations; while for the 6 model groups, rats are kept by 1 rat per cage, which is randomly applied with one from 6 different simulations including damp bedding (bedding: g, water: ml), ice water swimming (4 °C, 5 min), heat stress (45 °C, 5 min), all-day illumination (24 h), water deprivation (24 h), food deprivation (24 h), wherein it is worth noting that in the 18 consecutive days of medication period, a random simulation is given per day, and no same simulation should be arranged in 2 consecutive days. From the 1st day after simulation, open field is tested to observe stand-up times and horizontal move distance of all groups of rats. From the second day after simulation, forced swimming test is given to measure the immobility time within 4 days. From the 3rd or 4th day from simulation, sugar consumption experiment, prior to which 12 h of water deprivation is conducted, is given to measure 1% sugar water intake within 24 h of food deprivation.

At 2 h after final gavage (food deprivation for 15 h), draw the blood from the eyeball of the rat and measure the content of estradiol (E2 and testosterone (*T*) according to the instruction of test kits. Extricate brain homogenate and measure the content of methylepinephrine (NE), dopamine (DA), 5-hydroxytryptamine (5-HT) according to related instruction of test kits; extirpate uterus and remaining 20% ovarian tissue, extricate hypothalamus and hypophysis, and then fix the left side of the hypothalamus, hypophysis, uterus, and ovary in 10% formaldehyde solution before being processed into paraffin embedding sections to measure the expression of estrogen receptor (ER) in hypothalamus, hypophysis, uterus, and ovary, as well as the expression of AR in hypothalamus and hypophysis using the immunohistochemical method. On the other hand, store the right side of the hypothalamus in −80 °C refrigerator and measure the expression of ERmRNA using the RT-PCR method.

2.4. Statistical processing method

Data are statistically processed and analyzed using SPSS17.0 medical statistical package, and measurement data are expressed by mean value ± standard deviation ($\bar{x} \pm s$). One-way analysis of variance is performed for each group, wherein those of equal variance are tested by the LSD method, while those of heterogeneous variances are tested by the Games-Howell method.

3. Results

3.1. Effect on the behaviors of perimenopausal rats with depression

Effect on open-field test of perimenopausal rats with depression, and the results are shown in Table 1.