Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Medicine

journal homepage:www.elsevier.com/locate/apjtm

Document heading doi: 10.1016/S1995-7645(14)60082-1

Protective effect of topiramate on hypoxic-ischemic brain injury in neonatal rat

Hong Jiang*, Juan-Juan Lei, Yi-He Zhang

Neonatal Department, Affiliated Hospital of Yan´an University of Shaanxi Province , Yan´an 716000, Shaanxi, China

ARTICLE INFO

Article history:
Received 10 December 2013
Received in revised form 15 January 2014
Accepted 15 May 2014
Available online 20 June 2014

Keywords:
TPM
Brain Injury
NSE
GABA

ABSTRACT

Objective: To explore protective effect of topiramate (TPM) on hypoxic-ischemic brain injury. **Methods:** A total of 360 neonatal rats were selected then randomly divided into sham operation group, ischemia and hypoxia group, conventional treatment group and degradation therapy group (n=90). After surgical treatment, sham and ischemic hypoxia group were treat with normal saline; conventional treatment group was received TPM solution 100 mg/kg, 2 times/d; degradation therapy group received TPM solution 150 mg/kg, 2 times/d, per 3 d treatment each dosage was reduced 50 mg/kg, the lowest reduced to 50 mg/kg. Four groups received continuous treatment for 10 d. After treatment for 1 d, 4 d, 7 d, 10 d the cerebral edema, neuron-specific enolase (NSE) and γ-aminobutyric acid (GABA) levels and cognitive abilities of four groups were observed. **Results:** After 1 d, 4 d of treatment, the brain water content and NSE levels in ischemia and hypoxia group, the conventional treatment group and the degradation therapy group were significantly higher than that in sham group (P<0.05), the brain water content and NSE levels of the conventional treatment group and the degradation therapy group were significantly lower than that in the ischemic hypoxia group (P<0.05). GABA levels and learning ability of the ischemia and hypoxia group, the conventional treatment group and degradation therapy group were significantly lower than the sham group (P<0.05), the GABA levels and learning ability of the conventional treatment group and degradation therapy group were significantly higher than the ischemia and hypoxia group (P<0.05). After 7 d, 10 d of treatment, the brain water content and NSE levels in the sham operation group, the conventional treatment group and degradation therapy group were significantly lower than the ischemia and hypoxia group (P<0.05), while the GABA levels and learning ability of these three groups were significantly higher than that in the ischemia and hypoxia group (P<0.05), the GABA levels in the conventional treatment group were significantly higher than degradation therapy group (P<0.05); After 10 d of treatment, the GABA levels of the conventional treatment group were significantly higher than the sham group, the learning ability of the degradation therapy group and sham operation group were significantly higher than the conventional treatment group (P<0.05). **Conclusions:** The correct amount of short-term TPM has protective effect on hypoxic-ischemic brain injury, but long-term or excessive use may cause new damage to the brain and reduce the cognitive ability.

1. Introduction

Neonatal hypoxic-ischemic brain damage (HIBD) is a relatively common malignant complications caused by clinical perinatal asphyxia[1,2]. After brain injury, there will be brain edema, functional damage of nerve cells and nerve cell apoptosis[3,4] and other serious consequences. Improper treatment will become a major obstacle to the development of the nervous system of the neonatal, resulting in children mental retardation, epilepsy and cerebral palsy and other serious neurological disease. Serious patients will lead to death[5]. How to protect the cranial nerve of neonatal hypoxic-ischemic brain injury and promote the recovery of nerve cell function has been a research topic for medical workers. But HIBD pathogenesis is still inconclusive and its treatment is still not effective[6], the effect is not ideal. In

*Corresponding author: Hong Jiang, Ph.D., Chief Physician / Associate Professor, Neonatal Department, Affiliated Hospital of Yan'an University of Shaanxi Province , Yan'an 716000, Shaanxi, China.
Tel: 13809113078
E-mail: yiyunshanxi@aliyun.com
Foundation project: It is supported by Social Development Science and Technology Research Projects of Shanxi Province (2011 ks-30).

this study, we observed the effect of TPM different dose on hypoxic-ischemic brain injury in neonatal rats, in order to seek more effective treatment for HIBD.

2. Materials and methods

2.1. Animal grouping

A total of 360 7 d neonatal rats provided by the Experimental Animal Center of Medical College of Xi'an Jiaotong University were selected, weighting 12-16 g. They were randomly divided into sham operation group, ischemia and hypoxia group, the conventional treatment group and degradation therapy group (n=90).

2.2. Methods

2.2.1. Established models

Rats in the ischemia and hypoxia group, the conventional treatment group and degradation therapy group received 10% concentration of chloral hydrate 3 mg/kg intraperitoneal anesthesia and fixed in the operation board at the supine posture; under a 2 mm middle anterior neck incision and extended 1 mm to the right, after blunt separation of bilateral common carotid arteries and right commonjugular veins, proximal end of arteries and the distal end of the veins was ligated, and 2 mL 2.5 μ/mL heparin saline was infused. Then 20% blood in rats were drawn out to make ischemia, after 20 min they received blood infusion and the incision was sutured. The rats were exposed to 8% oxygen-92% nitrogen gas mixture for 2 h[8]. In Sham group only the vascular was isolated after anesthesia without ischemia and hypoxia treatment.

2.2.2. Topiramate (TPM) treatment

After the treatment, the sham group and ischemic hypoxia group received saline by gastric perfusion. The conventional treatment group were given with 2% TPM (Xian-Janssen Pharmaceutical Ltd., batch number: 080121230, size: 25 mg/tablet) by gastric perfusion, 100 mg/kg, 2 times/d; degradation therapy group received TPM solution 150 mg/kg, 2 times/d, per 3 d treatment each dosage was reduced to 50 mg/kg, the lowest reduced to 50 mg/kg. Four groups received continued treatment for 10 d, with the same volume of gavage solution.

2.2.3. Specimen collection

After treatment of 1 d, 4 d, 7 d, 10 d, 20 rats in each group were randomly selected and Y-type water maze was used to test their learn ability, then the brain tissue was obtained to detect cerebral edema and neuron-specific enolase (NSE) and γ-aminobutyric acid (GABA) levels.

Y water maze was applied to determine the ability of learning and memory. The water maze was consisted of a diameter 130 cm, height 50 cm circular pool and a "Y-type" device. "Y-type" device had a 40 cm long arm track and two short 15 cm arm, the top of one short arm was a resting platform for young rats, the other short arm had underground passage and the top was unobstructed. During the test, the depth was 30 cm and temperature was (25±1.2) ℃, the outer wall was pasted with reference. Rats were put into the water with the back towards of the "Y-type" device. Young rats climbed to the crossroad of "Y-type" device was recorded as one exercise, continue to exercise after break for 30 s. Rats had exercise 10 times in a group. When nine times of a group reached the standards of exercise, the total number of exercise minus 10 times was used as training times. All the training times were recorded to reach the required standard; the average number was used as training times. The less training times, the stronger learning ability of young rats[9].

2.2.5. Determination of brain water content[10]

10 rats of each group received 10% chloral hydrate 3 mL/kg anesthesia by intraperitoneal injection[11], the brains were removed after cardiac perfusion of saline. Rhinencephalon and hindbrain was removed, wet weight of brain tissue was measured by electronic scales (accurate to 1 mg, temperature 25 ℃, humidity 65%). They were placed at 80 ℃ thermostatic drying chamber drying, constant weight (2 times measured value difference <0.2 mg) was measured dry weight, brain water content (%) = (wet weight - dry weight) / wet weight × 100%.

2.2.6. NSE and GABA levels detection

Another 10 rats of each group were selected and the cardiac blood were collected after the anesthesia, the NSE serum levels[12] were detected with double-antibody sandwich assay. NSE determination steps were as follows: Samples were fully integrated with NSE antibody on the coated ball, then combined with 125I anti-NSE to form immune complexes, determined the pulses of coated ball by immune counter as the NSE content. The animals were fixed by cardiac perfusion and the brain was obtained. Concentration 40 g/L paraformalde was placed for 2 h and in distilled water for 4 h. Fixation, dehydration, transparence, waxing and embedding were carried out. GABA was detected by SABC markers[13]. All Ⅰ antibody, anti-Ⅱ poly peptides were purchased from Shanghai Biological Technology Co. BX-51 optical microscope (Olympus, Japan produced) was used to observe hippocampus CAl region slices. In each slice the average of positive cells was taken from 3 visions and expressed as positive neurons/high-power vision.

Download English Version:

https://daneshyari.com/en/article/3455404

Download Persian Version:

https://daneshyari.com/article/3455404

Daneshyari.com