

Plasma L-ENK, AVP, ANP and serum gastrin in patients with syndrome of Liver-Qi-stagnation *

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Abstract

AIM To investigate the pathophysiologic basis of syndrome of Liver-Qi stagnation and parameters for clinical differentiation.

METHODS Plasma L-ENK, AVP, ANP and serum gastrin were determined by RIA in 84 patients with neurasthenia, mastodynia, chronic gastritis, and chronic cholecystitis presenting the same syndrome of Liver-Qi stagnation in traditional Chinese medicine (TCM). Healthy subjects served as controls in comparison with patients having the same syndrome but with different diseases.

RESULTS Among the patients with Liver-Qi stagnation, the plasma L-ENK, ANP and gastrin levels were $38.83 \text{ ng/L} \pm 6.32 \text{ ng/L}$, $104.11 \text{ ng/L} \pm 29.01 \text{ ng/L}$ and $32.20 \text{ ng/L} \pm 6.68 \text{ ng/L}$, being significantly lower than those in the healthy controls ($P < 0.01$, $t = 3.34, 6.17, 4.48$). The plasma AVP of the patient group ($52.82 \text{ ng/L} \pm 19.09 \text{ ng/L}$) was significantly higher than that of the healthy controls ($P < 0.01$, $t = 5.79$). The above changes in patients having the same symptom complex but different diseases entities showed no significant differences, $P > 0.05$.

CONCLUSION The syndrome of Liver-Qi stagnation is closely related to the emotional regulatory abnormality of the brain, with decrease of plasma L-ENK, ANP and gastrin, and increase of plasma AVP as the important pathophysiologic basis.

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INTRODUCTION

Liver-Qi stagnation syndrome is common in liver disease. The predominant clinical manifestations were characterized by emotional alterations and digestive disturbances. In order to explore the pathophysiological basis and indexes of differentiation, we investigated the alterations of neurohumoral parameters in association with modulating emotional and digestive function.

MATERIALS AND METHODS

Subjects

Fifty-four patients with Liver-Qi stagnation syndrome selected from Xiangya Hospital and several general hospitals of Hunan Province from May 1995 to October 1996 were examined for plasma L-ENK, AVP and ANP. Seven were males and 47 females. Age ranged from 14-60 years, averaging 39 ± 11.2 years. The diagnoses were mastodynia (19), neurasthenia (17), chronic gastritis (10), and chronic cholecystitis (8). Another 30 patients selected from Xiangya Hospital through March 1997 to October 1997 were added, they were all females, aged 20-53 years, averaging 34.7 ± 12.7 years. Mastodynia was diagnosed in eleven cases, neurasthenia in nine cases, chronic gastritis in seven, and chronic cholecystitis in three.

The healthy controls were selected from the blood donors and employees in our hospital, all of them were negative in physical examination, blood routine, liver function test and chest fluoroscopy to rule out organic disease of heart, liver, lung, kidney, and nervous system diseases. L-ENK, ANP and AVP were detected in 30 cases, whereas serum gastrin was examined in 33 cases.

Differentiation and diagnosis by TCM

Based on previous criteria derived by our department^[1], they were modified according to the clinical epidemiological survey as: hypochondrial, breast and lower abdominal pain; depression; restless and easily irritated; obstruction sensation at the pharynx; dysmenorrhea, amenorrhea, or irregular menstrual cycle; and the tense pulse. The patients presented with 3 or more of the above six items were considered to have Liver-Qi stagnation syndrome. (The disease entities selected including mastodynia, neurasthenia, chronic gastritis, chronic cholecystitis

were diagnosed according to the textbook listed criteria and diagnosed by the departments of breast disease, neurology, general surgery, and digestive medicine).

Laboratory methods

All the 4 parameters were determined by radioimmunoassay. The apparatus used was FJ-2008 P-type gamma immunocounter. Venous blood samples were collected during fasting in the morning and determined subsequently. Radioimmunoassay kits for L-ENK and AVP were provided by the Department of Neurobiology of the 2nd Military Medical University, and the ANP and gastrin immunoassay kits were provided by Northern Institute of Immunoreagents, Beijing. The standard curve for L-ENK was $r = 0.998$, $CV = 3.07\%$, $RER = 0.039$; for ANP, $r =$

0.998 , $CV = 7.15\%$, $RER = 0.035$; for AVP, $r = 0.998$, $CV = 3.15\%$, $RER = 0.039$; and for gastrin, $r = 1.000$, $CV = 3.18\%$, $RER = 0.038$; all fitted the quality control criteria.

Statistical analysis

All data were expressed as $\bar{x} \pm s$. Student's t test and F test were used for comparison between groups 2 and 3.

RESULTS

Table 1 lists the results of measurement of plasma L-ENK, AVP, ANP and serum gastrin of the Liver-Qi stagnant patients group (LQSP) and of the normal controls and Table 2 shows the results of measurements in patients with different disease entities.

Table 1 The plasma L-ENK, AVP, ANP and serum gastrin levels in Liver Qi stagnation patients

Group	L-ENK	AVP	ANP	Gastrin
LQSP	38.83±6.32(40) ^b	52.82±19.09(30) ^b	104.11±29.01(32) ^b	32.20±6.68(30) ^b
Control	45.19±9.58(30)	29.88±10.35(30)	149.50±28.89(30)	47.02±15.64(30)

In brackets are the number of cases; ^b $P < 0.01$, vs control.

Table 2 The plasma and serum neurohumeral parameters of patients with Liver Qi stagnation syndrome of different disease entities

Group	L-ENK	AVP	ANP	Gastrin
Neurathenia	40.72±17.18(14)	42.95±1078(8)	110.24±39.40(10)	31.03±7.79(9)
Mastodynia	36.40±21.12(10)	61.31±23.57(13)	104.73±34.43(13)	33.49±7.08(11)
Gas-Chole*	40.87±26.02(16)	49.32±12.85(9)	99.83±20.15(9)	31.24±4.52(10)
<i>F</i> value	0.15	2.28	0.24	0.40
<i>P</i>	>0.05	>0.05	>0.05	>0.05

Note: in the brackets are the number of cases; *Gas-Chole stands for chronic gastritis and chronic cholecystitis.

DISCUSSION

In TCM, the function of liver is mainly dredging and storing of blood. The dredging function of the liver is extremely important in regulating the flow of Qi and blood in the body, the psychoemotion, digestion and absorption, water and fluid metabolism, menstruation and reproductive function. Psychoemotional disturbance is the main cause of Liver-Qi stagnation, and in turn, psychoemotional change is the clinical feature of Liver-Qi stagnation, such as easily irritated and arousal of angry, depression and sighing, insomnia with nightmares, even suspicious and indifferent and grieving. RIA of the psychoemotional and digestive function related neurohumoral parameters in this series showed that among the Liver-Qi stagnation patients, plasma L-ENK, ANP and serum gastrin were significantly decreased and the plasma AVP increased as compared with

those of the normal controls. However, between the different disease entities of various organ systems in modern Western medicine observed no significant difference. It strongly indicates that these alterations are the pathophysiological basis of Liver-Qi stagnation in common. These parameters are the indexes of syndrome, rather than the indexes of the disease entity. This study preliminarily explored the relationship between Liver-Qi stagnation syndrome and the modulatory neurohumeral factors associated with psychoemotional changes.

L-ENK is an active neuropeptide, its secretory neurons are distributed in the thalamic body thalamus, periaqueductal gray matter, and dorsal glial region of spinal cord, and are the modulators of emotional activity within the central nervous system^[2]. Gastrin is a gastrointestinal hormone secreted by G cells distributed in pylorus and upper duodenum.

Recent study reveals that some of the gastrointestinal peptide is also situated in CNS, the dual distribution of these peptides were called as brain enteric peptide^[3]. Immunohistochemical studies demonstrated that gastrin and leucine enkephalin are also presented in the brain, stomach, intestine and pancreas^[4]. Enkephalin is extensively distributed in the central nervous system and the digestive tract, and its secretory cells coincided with gastrin secretory cells^[5]. In this study, both plasma L-ENK and serum gastrin were significantly decreased in the patients with Liver-Qi stagnant syndrome, which might play an important role in the pathogenesis of psychoemotional modulation disorder and result in unstable emotional activity. Since the brain-enteric peptide secretion and release are closely related with the functional status of CNS and the vegetative nervous system, decreased brain-enteric peptide during Liver-Qi stagnation would certainly affect the gastric acid secretion, the intestinal, pancreatic juice, bile secretion and motility of the digestive tract, ultimately leading to digestive disturbance.

Vasopressin, the antidiuretic hormone (ADH), is synthesized by the neurons of supraoptic nucleus of hypothalamus. Release of ADH is normally modulated by plasma osmotic pressure, blood volume and blood pressure; but pain, vomiting and emotional tension may promote ADH release, and antagonize the diuresis^[4].

Atrial natriuretic polypeptide is mainly distributed in the brain, which is high in the hypothalamus and the diaphragmatic sellae region. Its secre-

tion is influenced by physical, humoral and neural factors. Its functions include natriuresis, vasodilation, and decrease of blood pressure^[6]. It was reported that ANP significantly inhibited the release of AVP via hypothalamus-neurohypophyseal axis, the antagonistic effect of ANP and renin-angiotensin not only existed peripherally, but also in the CNS, particularly in regulating the blood volume, electrolyte balance and maintenance of blood pressure^[7]. Decrease of plasma ANP and elevation of AVP might be one of the pathophysiologic basis of the CNS regulatory dysfunction resulting in increased vascular tension, sodium and water retention, and hypertension in Liver-Qi stagnation syndrome. But the cause-effect relationship, the precise mechanism of the elevated AVP and decreased ANP, as well as the validity of the four neurohumeral parameters in this study as reference indexes in differentiation of the Liver-Qi stagnant syndrome await further clarification.

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