

Correlation between Blood cAMP, cGMP Levels and Traumatic Severity in the Patients with Acute Trauma and Its Clinical Significance

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Summary: In order to investigate the correlation between traumatic severity and blood cAMP and cGMP levels in the patients with acute trauma and its clinical significance, 120 cases of trauma were randomly selected and divided into 4 groups ($n = 30$ in each group): mildly traumatic group (ISS = 9), moderately traumatic group (ISS = 10—16), severely traumatic group (ISS = 17—25) and dangerously traumatic group (> 25). The cAMP and cGMP levels were assayed in sera, leucocytes and platelets respectively in 6 h and 24 h after trauma. The results showed that cAMP and cGMP levels were elevated significantly in sera and platelets ($P < 0.05$ or $P < 0.01$), meanwhile cGMP levels in leucocytes ($P < 0.05$). It was concluded that cAMP and cGMP might play an important role in traumatic stress, participate in the cellular signal transduction and promote the immune function of leucocytes and the coagulation function of platelets. Serum cAMP and cGMP levels were upregulated correspondingly as ISS increased, and positively correlated to the traumatic severity.

Key words: cAMP; cGMP; trauma

At present, there are many methods used to assess the severity of trauma, such as AIS-ISS, TS, RTS, ASCOT, PHI and so on, in terms of the injury of anatomic regions, changes in pathophysiology, ages etc., but not involving the changes of stress responses of whole body at cellular and molecular levels following trauma. In this study, the changes of cAMP and cGMP in sera, leucocytes and platelets in the patients with acute trauma were investigated to explore their relations to the traumatic severity and clinical significance.

1 MATERIALS AND METHODS

1.1 Clinical Data

120 patients with acute trauma treated in our department, 79 males and 41 females, ages ranging from 18 to 60 years old (mean 37.8 ± 10.4) were randomly selected. Those having various acute or chronic diseases and inherited diseases were excluded from this study. Thirty healthy volunteers served as control group.

1.2 Trauma Grouping

All 120 patients with acute trauma were divided into 4 groups by using AIS-ISS ($n = 30$ in each group): mildly traumatic group (ISS = 9), moderately traumatic group (ISS = 10 - 16), severely traumatic group (ISS = 17 - 25) and dangerously traumatic group (> 25).

1.3 Sampling and Detection

Six h after trauma in each group, in addition 24 h after trauma in moderately traumatic group and severely group, venous blood was collected for count and classification of leucocytes. Serum, leucocytes

and platelets were isolated and cryopreserved at a freezing refrigerator. By using radioimmunoassay, the cAMP and cGMP levels in sera, leucocytes and platelets were determined with the kit provided by Laboratory of Radioimmunology, Shanghai College of Traditional Chinese Medicine (no 24-h group in dangerously traumatic group because of some patients not surviving for 24 h and in mildly traumatic group).

1.4 Statistical Analysis

The experimental results were statistically analyzed by commonly used medical statistical methods (analysis of variance and t test) and the data were expressed as $\bar{x} \pm s$.

2 RESULTS

2.1 Serum cAMP and cGMP Levels and Their Ratio (cAMP/cGMP) Changes in the Patients Following Trauma

The results were shown in table 1.

In 6 h after trauma, serum cAMP and cGMP levels were positively correlated with the severity of trauma. There was no significant difference between the mildly traumatic group and control group, but there was significant or very significant difference between moderately or severely or dangerously traumatic group and control group ($P < 0.05$ or $P < 0.01$). Twenty-four h after trauma, cAMP and cGMP levels were decreased to normal levels in the moderately traumatic group and severely traumatic group, with the difference being not significant as compared with control group, but the difference being very significant as compared with 6-h group ($P < 0.05$). The ratio of cAMP/cGMP was significantly increased in dangerously traumatic 6-h group as compared with control group ($P < 0.05$). However, in the moder-

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ately and severely traumatic 24-h group, the ratio of cAMP/cGMP was markedly decreased as compared with control group ($P < 0.05$).

2.2 cAMP and cGMP Levels in Leucocytes and the Changes in cAMP/cGMP Ratio Following Trauma

The results were shown in table 2.

Table 1 Serum cAMP and cGMP levels (10^9 mol/L) and changes in cAMP/cGMP ratio

Groups	cAMP	cGMP	cAMP/cGMP
Normal	20.00 \pm 0.57	3.14 \pm 0.13	6.73 \pm 0.41
Mild 6-h	16.60 \pm 1.60	4.28 \pm 0.47	4.82 \pm 0.63
Moderate 6-h	34.82 \pm 3.50 *	5.62 \pm 0.44 *	6.89 \pm 0.72 *
Severe 6-h	35.95 \pm 2.68 **	6.33 \pm 0.64 *	7.59 \pm 0.88 *
Dangerous 6-h	48.19 \pm 5.39 **	7.46 \pm 0.88 *	8.54 \pm 1.16 *
Moderate 24-h	14.82 \pm 0.66	4.44 \pm 0.29	3.98 \pm 0.56
Severe 24-h	17.50 \pm 1.75	5.36 \pm 0.79	4.20 \pm 0.54

* $P < 0.05$, ** $P < 0.01$ as compared with control group; $P < 0.05$ as compared with 6-h group

Table 2 Changes of cAMP and cGMP levels (10^9 mol/L) in leucocytes and the changes in cAMP/cGMP

Groups	cAMP	cGMP	cAMP/cGMP
Normal	1.83 \pm 0.33	0.23 \pm 0.02	8.27 \pm 0.66
Mild 6-h	2.40 \pm 0.67	0.37 \pm 0.05 *	7.04 \pm 1.12
Moderate 6-h	2.66 \pm 0.62	0.39 \pm 0.07 *	8.32 \pm 1.09
Severe 6-h	4.17 \pm 1.38	0.47 \pm 0.10 *	9.07 \pm 1.42
Dangerous 6-h	3.07 \pm 0.77	0.40 \pm 0.04 *	7.20 \pm 1.07
Moderate 24-h	2.17 \pm 0.28	0.54 \pm 0.08 *	6.12 \pm 0.86
Severe 24-h	2.20 \pm 0.38	0.37 \pm 0.07 *	8.03 \pm 1.13

* $P < 0.05$ as compared with control group

There was no significant difference in cAMP levels of leucocytes at different time points following trauma among the groups ($P > 0.05$), but cGMP levels were increased at different time points in the traumatic groups as compared with the control group

($P < 0.05$). There was no significant difference in cAMP/cGMP ratio among the groups ($P > 0.05$).

2.3 cAMP and cGMP Levels in Platelets and the Changes in cAMP/cGMP Ratio

The results were shown in table 3.

Table 3 cAMP and cGMP levels in platelets (10^{12} mol/L) and the changes in cAMP/cGMP ratio

Groups	cAMP	cGMP	cAMP/cGMP
Normal	7.48 \pm 0.83	1.47 \pm 0.40	7.56 \pm 0.94
Mild 6-h	6.68 \pm 0.79	1.86 \pm 0.18	4.03 \pm 0.45 *
Moderate 6-h	19.67 \pm 4.40 *	3.35 \pm 0.40 *	5.75 \pm 1.02 *
Severe 6-h	53.89 \pm 20.15 *	3.75 \pm 0.44 *	11.74 \pm 2.50 *
Dangerous 6-h	20.71 \pm 3.97 *	4.33 \pm 0.39 *	4.78 \pm 0.78 *
Moderate 24-h	9.75 \pm 1.04	2.64 \pm 0.26	4.34 \pm 0.55
Severe 24-h	12.15 \pm 1.97	2.45 \pm 0.20	4.82 \pm 0.50

* $P < 0.05$ as compared with control group, $P < 0.05$ as compared with 6-h groups

In 6 h after trauma, cAMP and cGMP levels in platelets were obviously increased in moderately, severely and dangerously traumatic groups as compared with the control group ($P < 0.005$); In 24 h after trauma, cAMP and cGMP levels were significantly decreased, but higher than those in the control group ($P < 0.05$). The cAMP/cGMP ratio was elevated or lowered alternately.

3 DISCUSSION

CAMP and cGMP, as the second messengers of signal transduction in human body, widely exist in tissues, organs and blood, but are difficult to be di-

rectly determined in tissues and organs of human body. The measurement of extracellular cAMP and cGMP levels can conveniently reflect the changes of functions in tissues and organs of whole body and signal transduction. The observation of blood cAMP and cGMP levels can reveal the stress responses of whole body to the trauma; The determination of intracellular cAMP and cGMP levels in tissues and organs can present the function changes of some organs.

The physiological function of process that blood cAMP and cGMP are mainly released and secreted from tissue cells is unclear at present. Whether it is beneficial to the reduction of intracellular cAMP and cGMP contents or a signal to other cells is unknown.

It is certain that cAMP and cGMP play a very important role in the changes of cellular functions. cAMP and cGMP regulate the intracellular signal transduction via their changes in the levels and ratio. It is known that the roles mediated by cAMP and cGMP include inhibition or activation of phosphorylase, activity and synthesis of enzymes for glycogenesis and glyconeogenesis, promotion of the secretion of insulin and pituitary hormones etc., the changes in ionic migration and permeability on the cellular surface. In normal blood, cAMP content is about 20×10^{-9} mol/L and its some nucleotides are analyzed by phosphodiesterase and some eliminated from blood via glomerular filtration. Studies demonstrated that under physiological and pathological conditions such as exercise, pregnancy, hypertension, diabetes, asthma, liver diseases, thyroid diseases and mental disorders, the basic levels of serum cAMP and cGMP change.

In this study, the results indicated that 6 h after trauma, the serum cAMP and cGMP levels were positively correlated with the severity of trauma. High levels of cAMP and cGMP also demonstrated that the signal transduction via protein kinase A system after trauma was activated.^[2,3] So, the determination of blood cAMP and cGMP can not only reveal the stress responses of human body after trauma, but also the severity of trauma.

In the early stage after severe trauma, the peripheral blood leucocytes are obviously increased (data not shown), mainly neutrophils. The cAMP levels in leucocytes (mainly neutrophils) had no significant difference among the groups, while the cGMP levels in the traumatic groups were significantly higher than in the control group. After severe trauma, the changes in cyclic nucleotides in the leucocytes have significant effects on some functions of leucocytes. It has been evidenced that the materials that can in-

crease the cAMP level in leucocytes can not only inhibit the migration of leucocytes, but also suppress the phagocytosis, while those that can increase the cAMP level in leucocytes show the opposite actions. The results of this study elucidated that the cGMP levels were obviously increased in 24 h after trauma, suggesting that the chemotaxis and phagocytosis at the early stage of trauma might be enhanced, which were consistent with those reported by Liang et al.^[4-6]

Platelets play a very important role in hemostasis and coagulation. It was found in this study that except the mildly traumatic group, the remaining traumatic groups showed higher levels of cAMP and cGMP in platelets than in the control group ($P < 0.05$), suggesting that the functions of platelets after trauma were in the active state. The increase of cGMP was more significant than cAMP, suggesting the action of cGMP was predominant. cGMP can promote the entry of calcium into platelets, which is helpful to the coagulation of platelets.

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(Received Nov. 19, 2003)