Biomedical Research 2017; 28 (6): 2639-2642 *ISSN 0970-938X*
www.biomedres.info

Study on the platelet levels of 1009 infants and high risk infants with cerebral palsy and its clinical significance.

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Abstract

Objective: To investigate the platelet levels in the blood serum of infants and high risk infants with cerebral palsy (CP) at different ages in order to provide theoretical basis for early intervention of CP and prevention of secondary lesion.

Methods: Serum specimens of 1009 infants with CP and 296 healthy children were collected, and blood platelet counts of these children were analyzed and evaluated. According to the age, both groups were divided into 4 months ~ 1 year old, 1 year old ~ 2 years old and 2 years old ~ 4 years old, a total of three groups. All children were accepted blood routine examination. The equipment of blood routine examination was cytoanalyzer MEK-5108 k made in Japan.

Results: The platelet levels of infants with CP in different ages groups were as follows: 362.30 ± 104.696 (× 10^9/L), 316.59 ± 93.958 (× 10^9/L), and 271.87 ± 71.190 (× 10^9/L). Z is 89.415 among the three groups. There were statistical significance (P<0.001). The platelet levels of healthy children in different age groups were as follows: 339.57 ± 71.309 (× 10^9/L), 306.56 ± 66.658 (× 10^9/L), and 283.64 ± 64.284 (× 10^9/L). Z is 30.975 among the three healthy groups. There was statistical significance (P<0.001). The platelet level of children with CP and healthy children are reduced with age growing. But the platelet level of children with CP is visibly higher than that of healthy children.

Conclusions: Platelet count of children with CP was significantly increased which made contribution to the form of microthrombus, increased blood viscosity and reduced cerebral blood flow perfusion. Platelet levels in CP group were decreased with age growing. It was suggested that early intervention was adopted in the blood coagulation process when children with CP were young, which was beneficial to the rehabilitation of CP.

Keywords: Cerebral palsy; Platelet; Early intervention.

Accepted on November 07, 2016

Introduction

Cerebral palsy (CP) is starting from the pregnancy to the infancy, and based on the non-progressive brain lesions to change into basic and perpetual disease whose movement and posture can be abnormally changed, and its symptoms would appear before 2 years old. If movement disorders and abnormal posture of children with CP are not treated in time, it will lead to children with long-term or permanent disability. CP is one of the main diseases to bring about children's disability, which seriously affects the physical and mental health of children and brings a heavy burden to the family and the society [1]. CP in clinic is mainly divided into spastic type, involuntomotory type, ataxic type and mixed forms. The children with CP not only have movement disorders, but also may be accompanied by mental retardation, visual and hearing impairments, abnormal behavior and epilepsy. Although CP damage is not progressive, the abnormal changes of some factors in the recovery process of body will still cause secondary damage [2]. For example, it was found that the platelet levels of children with CP were high in the long-term treatment. It is common in the clinical report that the platelet level of children with hypoxic ischemic encephalopathy is abnormal [3,4]. There were some researches about platelet therapy [5]. The authors compared and analyzed the platelet count in CP group and normal group in order to clarify the changes of the platelet count in CP group.

Participants and Methods

Clinical data

One thousand and nine children with CP admitted in rehabilitation center and 296 healthy children followed up in health department of the Third Affiliated Hospital of Zhengzhou University were selected from April 2013 to June 2015. The profile in 1009 children with CP group was as follows: 738 male, 271 female; 711 cases of 4 months ~ 1 year old; 203 cases of 1 year old ~ 2 years old; 95 cases of 2 years old ~ 4 years old. The profile in 296 healthy children was as follows: 154 male, 142 female; 114 cases of 4 months ~ 1 year old; 106 cases of 1 year old ~ 2 years old; 76 cases of 2 year

old ~ 4 years old. There was no significant difference between the two groups in the general data (P>0.05).

Diagnostic criteria

According to the standards and classification the national children with CP conference made [6], the inclusion criteria and exclusion criteria are as follows: (1) the injury causing symptoms of cerebral palsy is static and non-progressive; (2) the lesions leading to movement disorder and abnormal posture are located in the head; (3) the symptoms appear under 2 years old; (4) except patients with disability in perception, epilepsy and other abnormalities; (5) except central dyskinesia caused by other reasons. According to the definition of high risk infants with CP in the practice of neonatology [7], high risk infants with CP refers to a newborn who is most likely to suffer from CP in fetal period, parturition stage and neonatal period. The head circumference, height, weight, mental and motor development of the children in normal group were examined in the health department of the Third Affiliated Hospital of Zhengzhou University, which was in normal range.

Experimental apparatus

Hematology analyzer MEK-18k made in Japan was employed to examine the blood routine of all subjects.

Data analysis

SPSS 16.0 statistical software was used to analyze the data. The comparison of rate adopted chi-square test, t test was adopted to compare measurement data, and rank sum test was used for ranked data. And when P was less than 0.05, the differences had statistical significance.

Results

Compared with normal group, platelet of patients in CP group was significantly increased. The amount of patients with platelet 500 × 10^9/L in CP group was obviously more than normal group (P<0.05) (Tables 1 and 2).

Table 1. *Comparison of the mean values of platelet between two groups (× 10^9/L).*

Groups	Cases	± s	t	P
CP group	1009	344.59 ± 104.114	5.903	<0.001
Normal group	296	313.39 ± 71.341		

Table 2. *Comparison of platelet count between CP group and normal group (× 10^9/L).*

Groups	≥500	499-400	399-300	299-100	X^2	P
CP group	7.93%	19.33%	35.20%	37.54%	33.022	<0.001
Normal group	0.68%	11.82%	42.57%	44.93%		

The statistical analysis results of CP group and normal group were showed in Tables 3 and 4. It is obvious in tables that the platelet levels of children in the two groups are decreased gradually with age growing. And the younger the children, the higher the platelet level were. The platelet levels of children with CP were obviously higher than those of healthy children at the same age. And the differences were significant (P<0.05). Patients in CP group between four months and one year old had the highest platelet level, which was not only significantly higher than that of normal children at the same age ($P=1.83\times10^{-9}<0.001$), but also higher than that of patients with CP at other ages (P<0.001). The platelet levels of patients between one and two years old in CP group were higher than normal group (P=0.0012<0.05). There was no significant difference in the platelet level of patients within two and four years old in the two groups (P=0.089>0.05).

Table 3. *Comparison of the mean value of platelet at different ages in CP group.*

Ages	Cases	± s	Z	P
4 months ~ 1 year old	711	362.30 ± 104.696	89.415	<0.001
1 year old ~ 2 years old	203	316.59 ± 93.958		
2 years old ~ 4 years old	95	271.87 ± 71.190		

Table 4. *Comparison of the mean value of platelet at different ages in normal group.*

Ages	Cases	±s	Z	P
4 months ~ 1 year old	114	339.57 ± 71.309	30.975	<0.001
1 year old~ 2 years old	106	306.56 ± 66.658		
2 years old ~ 4 years old	76	283.64 ± 64.284		

Discussion

The main function of platelet is to stop bleeding, maintain the integrity of the vessel wall and form a hemostatic thrombus. And when vessel wall is injured, the platelet enables fibrin clot to stop bleeding, which can keep the vessel unobstructed. The changes in the ultrastructure of platelets are used to reflect the changes in mass, which can lead to bleeding or thrombosis [8]. Blood flow perfusion in the head is not significantly enough at the early stage of animal (with CP) experimental study [9,10]. And it is also found that the abnormal platelet count plays quite an important role in insufficient blood flow perfusion at the early stage of CP in clinic [11,12].

Platelets play an important role in the rehabilitation of children with CP. The normal levels of platelets have obvious promoting effect on memory, language and so on. However, platelet levels evidently elevated will cause blood flow perfusion in the head, even micro thrombus. It was found that the platelet levels of children with CP were significantly increased in the clinical treatment [13]. Platelet levels elevation and especially platelet activation is obvious in early stage of brain damage. With the severity of brain injury growing, platelet activation is more obvious [14,15]. Thromboxane B2 is increased after platelet activation in stress process of children

with brain injury, leading to cerebral vascular spasm which results in the reduction of blood supply and further damage [16]. It has been proof that platelet activation plays a certain role in the development of neonatal rats' brain damage and delayed injury in the foreign animal studies. It has been reported that platelet activating receptor antagonists are adopted to treat brain injury, which has obtained satisfactory results. It shows in the Table 3 that the younger the age, the higher the platelets level are; the greater the effect of blood perfusion in the head, the earlier the clotting intervention could be taken. All these are more beneficial to rehabilitation [17].

It is easy to form thrombus when platelet levels are elevated. Activated platelets can produce TAX2 to cause platelet aggregation which leads to blood vessel micro thrombus [7]. The mean blood flow velocity of end-diastole of the middle cerebral artery and the anterior cerebral artery of children with CP is evidently slower than that of healthy children with the same age, and the vascular resistance of children with CP is increased [18]. Studies reveal that platelet activation can be adjusted by excitatory amino acid synapse, resulting in sodium and calcium influx which cause brain edema, irreversible damage, block mitochondrial oxidative phosphorylation, even ultimately lead to neuronal death [19]. At present, some studies show that platelet activating antagonists have obvious protective effect on nerves in the experiment of newborn rats. On the other hand, it also proves that the rise of platelet levels and platelet activation is harmful to the brain [20-22]. Of course, there is other coagulation factors [23] involved in the state of high coagulation of children with CP, which has been proved in the animal experiment that other coagulation factors play a role in blood coagulation. The next step is to study the effect of other clotting factors and the interaction between other clotting factors and platelets [8].

There are some scholars [5] pointing out that nutrition factors of platelet in veinous reinfusion can improve intelligence and speaking capacity of children with CP, because platelet plasma has a great potential in regeneration, regulation of blood vessels and injured tissue cells, and secretion of growth factors, such as insulin-like growth factor-1, transforming growth factor B, vascular endothelial growth factor and platelet derived growth factor. All these factors can repair nerve and promote the nerve regeneration. It was indirectly indicated in the paper that the increased platelet level in blood coagulation was a risk factor, but could promote the rehabilitation of children with CP, and guide us how to make good use of increase of platelet level.

Therefore, the study was carried out to investigate the clinical application of platelet level in the blood of children with CP which is obviously rising in the development of CP. The platelet level can be as the criteria diagnosing CP in clinics. With the development of study on platelet action and the correlation between clotting factors, monitoring the platelet levels has a guiding significance for the secondary injury and its treatment of patients with CP, such as the early anti-coagulation therapy, the application of platelet activating antagonist [24], and the use of nutrition factors of platelet extracted in the centrifuge to treat children with CP [5].

Conflict of Interest

All co-authors have seen and agree with the contents of the manuscript and there is no conflict of interest.

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