Effect of platelet and cryoprecipitation transfusion on coagulation function and therapeutic effect in obstetric patients with acute disseminated intravascular coagulation

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Abstract: Objective: To analyze the effect of platelet transfusion and cryoprecipitation on coagulation function and therapeutic effect in obstetric patients with acute disseminated intravascular coagulation (DIC). Methods: 62 DIC patients in our hospital were collected as subjects. Random number table was used to divide patients into platelet group (n = 31) and cryoprecipitation group (n = 31). Patients in platelet group were given platelet transfusion, and patients in cryoprecipitation group were given cryoprecipitation transfusion therapy. 4 mL of venous blood was drawn separately before transfusion (T0), 2 hours after transfusion (T1), 24 hours after transfusion (T2) and 48 hours after transfusion (T3). The activated partial thromboplastin time (APTT), prothrombin time (PT), plasma fibrinogen content (Fbg) and thrombin time (TT) were detected. The therapeutic effect and recovery time of coagulation function were recorded. Results: The platelet group APTT, PT, TT, cure rate, and coagulation function recovery time were significantly increased (P<0.001), and Fbg was significantly decreased (P<0.001). Conclusion: The effect of cryoprecipitation transfusion on obstetric DIC patients is better than platelet transfusion, and the effect on coagulation function is more remarkable. Cryoprecipitation is worth popularizing in clinic.

Keywords: Platelet, cryoprecipitation, disseminated intravascular coagulation, coagulation function

Introduction

Disseminated intravascular coagulation (DIC) refers to the common final pathway of coagulation disorders caused by various diseases, and it belongs to clinicopathologic syndrome [1]. DIC causes widespread formation of microthrombus, and it results in massive loss of platelets and coagulation factors, leading to systemic hemorrhage and microcirculatory failure [2]. DIC has the characteristics of rapid onset, rapid progress and no obvious hypercoagulation period, and the threat to human body is great [3]. Once the patient does not receive timely and effective treatment, DIC will directly cause systemic hemorrhage and death [4]. Therefore, the treatment of DIC has been a hot topic for a long time in clinic. With the development of medical technology and in-depth research, it has been proved that DIC is hemorrhage due to the consumption of a large number of coagulation factors during the course of disease, and secondary fibrinolytic antibody is caused. Therefore, for the treatment of DIC, timely supplementation of coagulation factors is very important to promote the recovery of blood coagulation function [5-7]. In recent years, with the continuous improvement of blood supply and transfusion technology, the treatment on DIC has achieved stable therapeutic effects [9].

Cryoprecipitation is one kind of component transfusion, and concentrated preparation is prepared by collecting fresh blood from healthy people, separating hemorrhagic plasma and gradually freezing plasma [10, 11]. Cryoprecipitation contains a large number of coagulation factors, and they can provide power for the normal operation of blood coagulation function for patients with reduced volume [12]. Currently, studies have confirmed that cryoprecipitation...
Effect of platelet transfusion and cryoprecipitation has a significant effect in the treatment of DIC [13, 14]. However, compared with traditional platelet transfusion, it is still controversial on which method is more suitable for DIC. Therefore, we compared the efficacy and the difference of coagulation function between platelet transfusion and cryoprecipitation, to explore which method is more suitable for the treatment of DIC, and to provide reference and guidance for future clinical practice.

Materials and methods

General data

62 DIC patients in our hospital were collected as subjects, and all patients were female. The ages of patients were between 22 to 34 years old, with an average age of 26.15 ± 4.22 years. Random number table was used to divide patients into platelet group (n = 31) and cryoprecipitation group (n = 31). Patients in platelet group were given platelet transfusion, and patients in cryoprecipitation group were given cryoprecipitation transfusion therapy. This experiment has been approved by the ethics committee of Jingzhou Central Hospital affiliated The Second Clinical Medical College, Yangtze University, and all the subjects signed informed consent.

Inclusion and exclusion criteria

Inclusion criteria: patients were in gestational period; patients conformed to DIC diagnostic standard [15]; patients were diagnosed as DIC by Department of Hematology and Department of Critical Care Medicine in our hospital; after diagnosis, patients continued treatment in our hospital; data of cases were complete; patients cooperated with the medical staff in our hospital; the ages of patients were 18~50 years old. Exclusion criteria: cancer patients; severe organ failure patients; patients with cardiovascular and cerebrovascular diseases; patients with pregnancy; patients with liver and kidney dysfunction; drug allergy patients; mental patients; patients with physical disabilities; patients who cannot take care of themselves; transferred patients.

Methods

Two groups of patients were given routine emergency treatment, including heparin and antifibrinolytic drugs. In cryoprecipitation group, 10 U of frozen platelet and 10 U of cryoprecipitation were infused rapidly, and red blood cell fluid was added according to blood loss. Observe whether there were clots during transfusion. If there was no clot, appropriate fibrinogen (2.0-2.5 g/L) could be supplemented according to body weight. The platelet group was given 10 U frozen platelet, and the transfusion dose was based on patient’s inspection results. All blood products used in this experiment were provided by local blood donor center.

Outcome measures

Coagulation function: 4 mL of venous blood was drawn separately before transfusion (T0), 2 hours after transfusion (T1), 24 hours after transfusion (T2) and 48 hours after transfusion (T3). Automatic coagulation analyzer and original kits were used to detect coagulation function, including activated partial thromboplastin time (APTT), prothrombin time (PT), plasma fibrinogen content (Fbg) and thrombin time (TT). Therapeutic effect: DIC rehabilitation guidelines were used to evaluate the effect after 48 hours [16]. If DIC symptoms disappeared completely, and coagulation function test results were completely normal, then it was evaluated to be cured. If DIC symptoms were significantly alleviated, and the improvement of coagulation function was more than 50%, then it was evaluated to be effective. If the results of DIC symptoms and blood coagulation function tests showed no significant improvement, or even deterioration happened, then it was evaluated to be ineffective. The cure rate = (the number of cure cases + the number of effective cases)/total number of cases ×100%. Recovery time of coagulation function: the total time from starting treatment to normal blood coagulation function was recorded.

Statistical methods

SPSS24.0 statistical software (from Beijing Sichuang Weida Information Technology Co., Ltd.) was used to calculate all the experimental results. Graphpad 8 (from Shenzhen Tianruiqi Software Co., Ltd.) software was used to draw all the graphics, and the results were checked twice. Counting data were expressed in the form of (rate), such as cure rate. Groups comparison was using Chi-square test. The data were showing in the form of mean ± standard deviation. Results at multiple time points were
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Comparison of general data

There was no significant difference in age, BMI, platelet, red blood cell, white blood cell, gestational age, smoking history, residence, educational background, times of pregnancy and exercise habits between two groups (P>0.05). It indicated that the general data of two groups were comparable (Table 1).

Comparison of coagulation function

There was no significant difference in APTT, PT, Fbg and TT at T0 and T1 between two groups (P>0.05). APTT, PT and TT at T2 and T3 in platelet group were significantly higher than those in cryoprecipitation group (P<0.05), and Fbg in platelet group was lower than that of cryoprecipitation group (P<0.05). In platelet group and cryoprecipitation group, APTT, PT and TT at T1 were all lower than values at T0 (P<0.05); APTT, PT and TT at T2 were lower than values at T1 (P<0.05), and APTT, PT and TT were the lowest at T3 (P<0.05). In both groups, Fbg at T1 was higher than Fbg at T0 (P<0.05), and Fbg at T2 was higher than Fbg at T1 (P<0.05), and it was the highest at T3 (P<0.05) (Tables 2-5 and Figures 1-4).

Comparison of therapeutic effects

In cryoprecipitation group, 58.06% cases (18 cases) were evaluated to be cured, 35.48%
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Table 3. Comparison of PT between the two groups (Reference value: 11~14 s)

<table>
<thead>
<tr>
<th></th>
<th>Platelet group (n = 31)</th>
<th>Cryoprecipitate group (n = 31)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>48.62 ± 25.93</td>
<td>49.13 ± 23.18</td>
<td>0.935</td>
</tr>
<tr>
<td>T1</td>
<td>43.17 ± 13.84</td>
<td>41.59 ± 14.86</td>
<td>0.666</td>
</tr>
<tr>
<td>T2</td>
<td>36.15 ± 9.86*</td>
<td>35.32 ± 11.30*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T3</td>
<td>30.58 ± 9.14*</td>
<td>29.24 ± 6.24*</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: *represents a comparison with the normal value of PT of T0. The PT of T2 and T3 in both groups is significantly higher than the normal value, *P<0.001.

Table 4. Comparison of Fbg between the two groups (Reference value: 2~4 g/L)

<table>
<thead>
<tr>
<th></th>
<th>Platelet group (n = 31)</th>
<th>Cryoprecipitate group (n = 31)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>1.26 ± 0.42</td>
<td>1.22 ± 0.46</td>
<td>0.722</td>
</tr>
<tr>
<td>T1</td>
<td>1.38 ± 0.62</td>
<td>1.40 ± 0.58</td>
<td>0.896</td>
</tr>
<tr>
<td>T2</td>
<td>1.59 ± 0.45</td>
<td>1.98 ± 0.62</td>
<td>0.006</td>
</tr>
<tr>
<td>T3</td>
<td>1.74 ± 0.35</td>
<td>2.63 ± 0.39</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 5. Comparison of TT between the two groups (Reference value: 11~17 s)

<table>
<thead>
<tr>
<th></th>
<th>Platelet group (n = 31)</th>
<th>Cryoprecipitate group (n = 31)</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>36.82 ± 8.14</td>
<td>37.05 ± 8.26</td>
<td>0.110</td>
<td>0.912</td>
</tr>
<tr>
<td>T1</td>
<td>32.73 ± 10.52</td>
<td>31.66 ± 9.72</td>
<td>0.416</td>
<td>0.679</td>
</tr>
<tr>
<td>T2</td>
<td>28.36 ± 5.94</td>
<td>24.68 ± 6.91</td>
<td>2.249</td>
<td>0.028</td>
</tr>
<tr>
<td>T3</td>
<td>26.93 ± 6.82</td>
<td>20.55 ± 5.60</td>
<td>4.025</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure 1. APTT comparison at different time points between two groups. a means APTT compared with same group at T0, P<0.05; b means APTT compared with same group at T1, P<0.05; c means APTT compared with same group at T2, P<0.05.

Activated platelets and their splitting products play an important role in maintaining normal blood coagulation. The fibrin and various coagulation factors in cryoprecipitation are beneficial to the release and adhesion of platelet factors, and the formation of thrombin can be accelerated [19]. Therefore, platelet and cryoprecipitate can both repair and maintain the normal coagulation function of patients with DIC [20]. The curative effect of platelet and cryoprecipitation on DIC has been confirmed, but domestic and foreign researches were mostly limited to the guidance of the two methods. For example, Piggozzi L et al. [21] proposed that the cure rate of platelet transfusion on DIC was about 80%. Philip [22] proved that the effect of cryoprecipitation can maintain normal coagulation function for 24 hours. In this paper, through rigorous inclusion and exclusion criteria, advanced statistical software, different statistical software for secondary checking and strict spirit of scientific research, curative effect and coagulation function under platelet transfusion and cryoprecipitate transfusion were compared.
The experimental results showed that there was no significant difference in coagulation function between two groups. The coagulation function of cryoprecipitation group was significantly better than that in the platelet group. It indicated that platelet transfusion and cryoprecipitation had good effect on coagulation function in DIC patients, but cryoprecipitation transfusion was more conducive to the recovery of coagulation function. The main reason for the difference in coagulation function is speculated that the mechanism of platelet transfusion therapy is to improve and maintain coagulation dysfunction by supplementing platelet. Some studies pointed out that the content of coagulation factor in whole blood is low, and the platelet dilution is small. If the coagulation factor is added by injecting whole blood, it will cause coagulation disorder [23]. Cryoprecipitation is a coagulation factor prepared by fresh frozen plasma. The main components are FXIII, von Willebrand factor and fibronectin. Among them, FXIII mainly promotes platelet aggregation and synthesis of endogenous thrombin by accelerating the activation of FX [24], and it can replace the effect of platelet transfusion in DIC treatment. Besides, Von Willebrand factor is a glycoprotein with adhesion function. It maintains the activity of FVIII in blood, and it also binds to the protein structure of platelet receptor. Von Willebrand factor mediates the adhesion and aggregation ability of platelets, and it accelerates the coagulation of blood [25]. Therefore, von Willebrand factor can be used as auxiliary in the process of cryoprecipitation transfusion. The most important activation factors in cryoprecipitation are maintained, and coagulation function is improved. Besides, the operation of platelets is accelerated, so that coagulation function is treated quickly. Fibronectin is a protein complex with regulatory activity. It has phagocytic capacity for senescent cells and bacterial foreign bodies [26]. This also enables DIC patients to disinfect wound through devouring reticular cell during cryoprecipitation. Compared with platelet transfusion, cryoprecipitation has higher safety. However, because the safety of two methods has not been investigated in this paper, we need further experiments to verify our conjecture.

The cure rate of cryoprecipitation group was 93.55%, and it was significantly higher than 74.19% of platelet group. The recovery time of coagulation function in cryoprecipitation group was significantly shorter than that of platelet
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Table 6. Comparison of therapeutic effects [n (%)]

<table>
<thead>
<tr>
<th></th>
<th>Platelet group (n = 31)</th>
<th>Cryoprecipitate group (n = 31)</th>
<th>( \chi^2 )</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure</td>
<td>10 (32.26)</td>
<td>18 (58.06)</td>
<td>5.321</td>
<td>0.032</td>
</tr>
<tr>
<td>Effective</td>
<td>13 (41.94)</td>
<td>11 (35.48)</td>
<td>2.358</td>
<td>0.057</td>
</tr>
<tr>
<td>Invalid</td>
<td>8 (25.81)</td>
<td>2 (6.45)</td>
<td>6.371</td>
<td>0.021</td>
</tr>
<tr>
<td>Cure rate (%)</td>
<td>74.19</td>
<td>93.55</td>
<td>4.292</td>
<td>0.038</td>
</tr>
</tbody>
</table>

Figure 5. The comparison of recovery time of coagulation function. a means recovery time compared with platelet group, P<0.001.

It is suggested that the effect of cryoprecipitation is better for DIC patients. However, cryoprecipitation usually requires a large dose in clinic, and the incidence of homologous immunity between blood-borne diseases and leukocyte system increases greatly [27]. Therefore, during cryoprecipitation transfusion, we need to pay more attention to blood quality and the operation of virus inactivation. Besides, the dosage should be strictly used according to actual clinical situation of patients.

The therapeutic effect and coagulation function of platelet transfusion and cryoprecipitation transfusion on DIC were compared in this experiment, but there are still some shortcomings due to limited experimental conditions. For example, the base of research subject was small, and subjects were relatively single, so statistical analysis of large data could not be carried out. Besides, the experimental time span was small, and long-term prognosis and the changes of coagulation function in two groups could not be evaluated. We will conduct follow-up surveys on subjects, expand sample size, and improve the experimental design. We will continue to explore the treatment of DIC in depth, to obtain the best experimental results.

In conclusion, the effect of cryoprecipitation on DIC patients is better than platelet transfusion, and the effect of cryoprecipitation on repairing coagulation function is more remarkable. So cryoprecipitation is worth popularizing in clinic.

Disclosure of conflict of interest

None.

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