Blood Components Therapy as a Preventive Strategy for Coagulopathy in High-Risk Obstetric Patients in a Tertiary Centre in North India - An Interventional Study

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ABSTRACT

BACKGROUND

Obstetric practitioners routinely deal with antenatal patients who have high risk of developing established coagulopathy, which leads to a very high incidence of maternal morbidity and mortality. We wanted to assess the role of blood components in preventing disseminated intravascular coagulation (DIC) in high-risk patients and determine the amount of blood components required along with the rate of improvement in the DIC score, during treatment of high-risk obstetric patients of DIC and in patients with established DIC.

METHODS

This is an interventional study. 274 obstetric patients who were at high risk for developing DIC and / or with established DIC admitted during the 20 months study duration were included in the study. Patients were categorized in to three groups based on the DIC score according to ISTH scoring system in to non-overt and overt DIC groups. Those with DIC score < 5 were grouped as IA and IB randomly and those with DIC score > / = 5 were grouped as II. Software used was ANOVA using variance ratio F test for testing the significance between groups and chi-square test was used to find out the association between the groups or parameter.

RESULTS

Prophylactic transfusion of blood components showed faster rate of improvement than control group. Average consumption of blood components was more in patients of established coagulopathy as compared to non-overt group.

CONCLUSIONS

Transfusion of blood components can prevent overt DIC in high-risk patients.

KEYWORDS

DIC - Disseminated Intravascular Coagulation, PPH - Post Partum Haemorrhage, Coagulopathy, Component Therapy

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BACKGROUND

Obstetric haemorrhage is the leading cause of maternal morbidity and mortality worldwide.[1] Blood transfusion is a life-saving procedure but an inappropriate usage of blood products in obstetric emergencies especially in cases of massive bleeding is associated with increased morbidity and risk of death.[2-4] Thorough knowledge of the aetiology, pathophysiology, and optimal therapeutic options of major obstetric haemorrhage may help to avoid lethal outcomes. In antenatal patients we deal with wide range of patients who are actually at risk of developing established coagulopathy which leads to very high incidence of maternal morbidity and mortality.

Disseminated intravascular coagulation (DIC) was first described by Joseph De Lee in 1901 as a fatal haemorrhagic diathesis following placental abruption.[5] In the last trimester of pregnancy, where the coagulation system is enhanced and the fibrinolytic system is suppressed, massive haemorrhage leads to consumption of coagulation factors, leading to further haemorrhage, forming a vicious cycle such as disseminated intravascular coagulation.[6-10] Clinically, DIC may lead to a wide range of manifestations from unnoticed intravascular thrombosis and microvascular damage to uncontrollable bleeding. DIC always evolves secondary to predisposing clinical condition.[11]

In 2001, the International Society on Thrombosis and Haemostasis (ISTH) Sub-Committee of the Scientific and Standardisation Committee (SSC) on Disseminated Intravascular Coagulation (DIC) proposed that the working definition of DIC be delineated into two phases. Non-overt DIC would represent subtle haemostatic dysfunction while overt DIC recognized its decompensated phase. It can originate from and cause damage to the microvasculature, which if sufficiently severe, can produce organ dysfunction.[12] Obstetric disorders associated with DIC include amniotic fluid embolism, placental abruption, retained products of conception, eclampsia, and abortion. Commonly described causes of DIC in obstetrics include amniotic fluid embolism,[13] intrauterine foetal demise,[14] HELLP syndrome, pre-eclampsia / eclampsia, placental abruption and placenta praevia, septic abortion and intrauterine infection, postpartum haemorrhage, acute fatty liver of pregnancy.

Retrospective studies have reported the incidence to range from 0.02 % to 0.07 % of all pregnancies.[15,16] Although the overall prevalence of DIC is low in pregnancy, the frequency of DIC in women with specific complications can be quite high.

There is no single laboratory test to diagnose DIC. The diagnosis is established based on clinical suspicion and supportive laboratory tests. The tests used include laboratory parameters indicative of procoagulant and fibrinolytic substance activation, inhibitor consumption and organ damage or failure.[17-19]

The International Society for Thrombosis and Haemostasis has adopted a score that assists in the diagnosis and the identification of patients at risk for the development of DIC.[12]

Scoring System for Overt Disseminated Intravascular Coagulation (DIC)

1. Risk assessment: does the patient have an underlying disorder known to be associated with overt DIC?
   If yes: Proceed.
   If no: Do not use this algorithm.
2. Order global coagulation tests (platelet count, prothrombin time, fibrinogen, fibrin related marker).
3. Score global coagulation test results.
   - Platelet count (> 100,000 / mm^3 = 0; < 100,000 / mm^3 = 1; < 50,000 / mm^3 = 2)
   - Elevated fibrin related marker (e.g. D-dimers; fibrin degradation products)
     (No increase = 0; moderate increase = 2; strong increase = 3)
   - Prolonged prothrombin time
     (< 3 s = 0; > 3 but < 6 s = 1; > 6s = 2)
   - Fibrinogen level
     (> 1.0 g / L = 0; < 1.0 g / L = 1)
4. Calculate score
   If ≥ 5: compatible with overt DIC: repeat score daily
   If < 5: suggestive (not affirmative) for non-overt DIC: repeat next 1 – 2 days.

The present study was conducted to determine and compare the amount of blood components required along with rate of improvement in the DIC score, during treatment of high-risk obstetric patients of DIC and in patients with established DIC. We also tried to determine the rationality of prophylactic blood component therapy.

METHODS

Present study is an interventional study. Study was performed after obtaining institutional ethical committee's approval. 274 obstetrical patients at high risk for developing DIC and / or with established DIC admitted during 20 months' duration, from January 2018 to August 2019 were included in the study. Antenatal patients with high-risk criteria for coagulopathy were selected for the study including patients with intrauterine foetal demise, pre-eclampsia and eclampsia, placental abruption, post-partum haemorrhage, intrauterine sepsis, post-abortal and postnatal cases of retained products of conception, antenatal and postnatal cases of established coagulopathy. Antenatal patients with inherited coagulopathy were excluded in the study.

All patients were explained about the two modalities of treatments out of which one will be given to them, and their risks and benefits. Written informed consent was taken from all the patients included in the study. These patients were categorised in to three groups based on the DIC score according to ISTH scoring system in to Non-overt and Overt DIC groups. Those with DIC score < 5 were categorised as IA and IB randomly and those with DIC score > / = 5 were selected as II. Group IA: high risk for acquired coagulopathy i.e., non-overt DIC (whole blood or packed red cells were transfused in severely anaemic patients). Group IB: high risk for acquired coagulopathy i.e. non-overt DIC (blood

components were administered) and group II (patients with established coagulopathy) were administered blood components i.e. packed red blood cells (PCV), fresh frozen plasma (FFP), and platelets.

Coagulation profile of the patients along with other routine investigations were done at the time of admission. Coagulation profile included prothrombin time, platelet count, S. fibrinogen levels, fibrinogen degradation products (FDP) and DIC score was calculated for each patient on day 1 and day 5 of admission. In established DIC patients (group II), coagulation profile was sent every 24 hours to look for improvement in coagulation profile as these were critically ill patients., but comparison of mean DIC score on day 1 and day 5 was considered. Blood samples were collected in 3.2 gm % trisodium citrate as anticoagulant in ratio of 9:1 and immediately centrifuged at 2500 g for fifteen minutes, Prothrombin time (PT), activated partial thromboplastin time (aPTT), Fibrinogen, D-Dimer and platelet count estimation was recorded.

Statistical Analysis

Statistical calculations were performed by software used for ANOVA using variance ratio F-test for testing the significance between groups and chi square test was used to find out the association between the groups or parameter.

RESULTS

Total patients (N = 274) were grouped into three groups based on DIC score according to ISTH scoring system in to Non-overt and overt DIC groups. Group IA included 126 patients, group IB included 116 patients and group II included 32 patients. Majority of the patients in each group, in our study belonged to rural areas. Common high-risk factors associated with overt DIC group II were post-partum haemorrhage (25 %) and abruptio placentae (18.7 %) while intrauterine foetal demise, pre-eclampsia and eclampsia were commonly associated with non-overt DIC.

Caesarean section (LSCS) (54.76 % and 57.76 % respectively) and vaginal delivery (23.02 % and 20.69 % respectively) constituted one of the major obstetrical interventions in patients of non-overt DIC group (IA and IB) while in patients of overt DIC group LSCS and vaginal delivery comprised only 25 % and 21.88 % respectively. However medical management played key role in 34.38 % cases of overt DIC group. Exploratory laparotomy and hysterectomy were required in 9.38 % cases each.

Whole blood transfusion was given in the Group IA patients, while in the other two groups only blood components (PCV, FFP, platelets) were administered. Mean number of blood components required in overt DIC (group II) patients were three times greater than that required in non-overt DIC (group IB) to correct the coagulation profile of patients (Table 1, 2, 3). Despite vigorous component therapy mortality in group II was 59.38 %.

Mean DIC score on day 1 of admission was similar in both groups but by day 5 the mean DIC score in group IA was 2.47 and group IB was 0.82 i.e. the rate of improvement was faster in group IB. On applying chi square test for degree of freedom (DOF) 1, P-value was 0.006, which shows the difference to be statistically significant (Figure 1).

Comparison between group IB and group II showed faster rate of improvement in group IA (Figure 2).

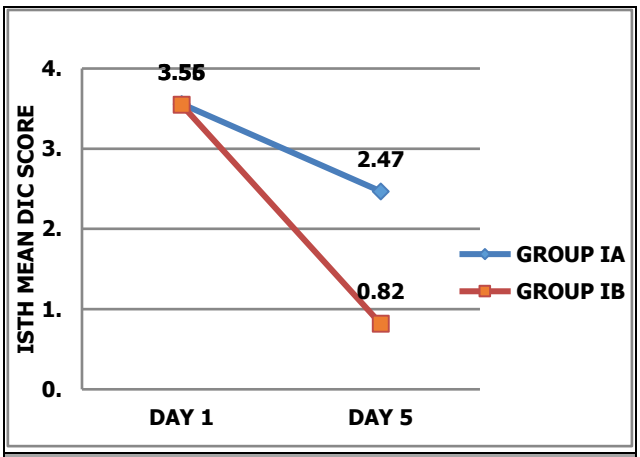

Figure 1. Trend of Improvement in DIC Score Over 5 Days in Group IA and IB

[Chi-square test for DOF = 1, P-value = 0.006]

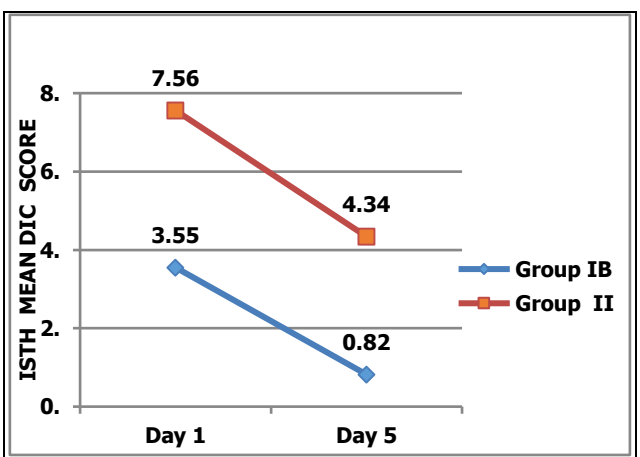

Figure 2. Trend of Improvement in DIC Score Over 5 Days in Group IB and II

[Chi-square test for DOF = 1, P-value = 0.003]

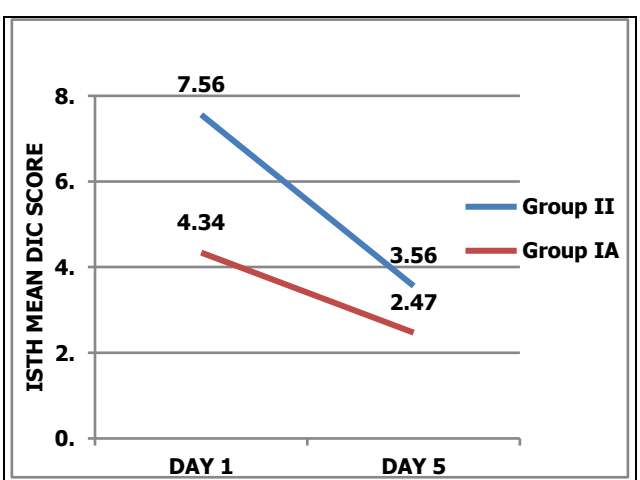

Figure 3. Trend of Improvement in DIC Score Over 5 Days in Group IA and II

[Chi-square test for DOF = 1, P-value = 0.085]

Group / Frequency of Whole Blood / PRBC Transfusion	0	1	2	3	4	5	Total	Mean +–SD	F	Lower Limit	Upper Limit
I A	78	25	21	02	0	0	126	0.57 +- 0.82	324.08	0.425422	0.714578
IB	0	85	22	09	0	0	116	1.34 +- 0.62	P < 0.0001	1.22597	1.45403
II	0	0	0	5	21	6	32	4.09 +- 0.59	Highly significant	3.88414	4.29586

Table 1. Frequency of Packed Cells / Whole Blood Transfused to Patients in Different Groups. Statistically Significant Difference is Observed in Frequency of PRBC / Whole Blood Transfusion Requirements between the Groups on 95 % C.I. of Mean

X^2 = 11.4833 Df = 2 P < 0.00320939, P < 0.05 significant

Group / Frequency of Platelets Transfusion	1	2	3	4	5	Total	Mean +–SD	F	Lower Limit	Upper Limit
IB	85	22	9	0	0	116	1.34 +- 0.62	469.554	1.22597	1.45403
II	0	0	10	0	22	32	4.37 +_ 0.94	P < 0.001	4.03109	4.70891

Table 2. Frequency of Platelets Transfused to Patients in Different Groups

F = 469.554 P < 0.0001, X^2 = 9.6433, Inference = Highly significant

Group / Frequency of FFP Transfusion	1	2	3	4	5	Total	Mean +–SD	F	Lower Limit	Upper Limit
IA	85	22	9	0	0	116	1.34 +- 0.62	469.554	1.22597	1.45403
II	0	0	10	0	22	32	4.37 +- 0.94	P < 0.001	4.03109	4.70891

Table 3. Frequency of Fresh Frozen Plasma (FFP) Transfusion in Different Groups

X^2 = 9.6433 Df =1

On comparing the trend of improvement in DIC score in group IA and group II the result showed the difference to be statistically insignificant as on applying Chi-square test, for DOF 1, P-value was 0.085 (Figure 3). Results showed that in non-overt DIC groups (IA and IB), foetal survival was 30.95 % and 32.76 % respectively while in overt DIC group foetal survival was nil.

DISCUSSION

Majority of patients with non-overt DIC group (groups IA and IB) were managed by LSCS (54.76 and 57.76 % respectively) and vaginal delivery (23.02 % and 20.69 % respectively), in patients of overt DIC, LSCS and vaginal delivery was performed in 25 % and 21.88 % cases respectively. Exploratory laparotomy was performed in 9.38 % cases. Average number of blood components i.e. Packed cell volume (PCV), Platelets and Fresh frozen plasma (FFP) required in Overt DIC group II patients was three times higher than that required in non-overt DIC group IB patients to correct the abnormality in coagulation profile. Despite vigorous component therapy, mortality in group II was 59.38 % while in group IB there was no mortality. Prophylactic component therapy was beneficial in decreasing maternal mortality. The DIC score of all patients were calculated (as per ISTH scoring system) on day 1 and 5 of admission, then mean DIC score was calculated for all three groups for day 1 and day 5 of admission respectively and trend of improvement in mean DIC score was compared among all three groups.

- Group IA versus IB, the mean DIC score were similar to start with on day of admission but rate of improvement in score was faster in group IB in whom prophylactic component therapy was given. (P-value = 0.006, showed the association to be statistically significant.)
- Group IB versus II, the mean DIC score in group II was 7.56 _+ 0.5 while in group IB it was 3.55 +_ 0.5. In both groups blood components were given as per requirement but the rate of improvement in group IB was faster than overt DIC group. (P-value = 0.003, showed the association to be statistically significant).
- Group IA vs. II, the P-value showed the association to be statistically insignificant.

Maternal outcome analysis showed that in non-overt DIC group IA and IB, majority of the patients were managed in wards (62.70 % and 72.41 % respectively), while in overt DIC group II 100 % patients were managed in intensive care unit. Some patients of non-overt DIC were managed in high dependency units (HDU), 16.67 % (group IA) and 12.07 % (group IB) respectively. The outcome in group IB was better as only 13.79 % patients needed ICU care, none expired, and 93.10 % patients were discharged in satisfactory conditions. In group IA (control group) 20.63 % needed ICU care and maternal mortality occurred in 1.59 % cases and 90.48 were discharged in satisfactory condition. In group II (overt DIC) mortality was observed in 59.38 % cases, only 31.25 % were discharged in satisfactory conditions.

Analysis of the foetal outcome showed that in group IA and IB foetal survival was 39 % and 40.86 % respectively. However, in group II foetal survival was nil.

CONCLUSIONS

Better foetal and maternal outcome was observed with prophylactic component therapy in cases of non-overt DIC obstetric patients. Hence, blood bank facilities with component separation should be strengthened especially in rural areas to reduce maternal mortality rate.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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