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Original Research Article

Evaluation of appropriateness of packed red blood cell and fresh frozen plasma transfusion in post-surgical adult patients admitted in ICU and its outcome: a retrospective study in a tertiary care hospital

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ABSTRACT

Background: The objective of this study was to evaluate appropriateness of packed red blood cell (PRBC) and fresh frozen plasma transfusion (FFP) in post-surgical adult patients admitted in ICU and its outcome.
Methods: A total number of 800 ICU adult patients were enrolled. Out of these 600 patients received PRBC transfusion and 200 received FFP transfusions. Transfusion pattern was analyzed with respect to the number of units transfused, pre and post transfusion hemoglobin levels and coagulation profile. The outcome was measured in terms of mortality, morbidity and length of ICU stay. Transfusions were categorized into appropriate and inappropriate based on transfusion triggers used as per BSH guidelines (British Society for Hematology). The SPSS software was used for analyses.
Results: Out of six hundred, 384 were those with appropriate red cell transfusion. In the appropriate transfusion group, majority i.e. 167 (43.49%) underwent more units of PRBC transfusion. The mean duration of mechanical ventilation in appropriate group was 7.43±4.1 days and in inappropriate group was 5.95±3.34 days. ($p<0.05$). There was significant association found between the high mortality and appropriateness of blood transfusion. Out of 200, One hundred and thirty-seven (137) were those with appropriate FFP transfusion. Majority of the patients underwent two units of FFP transfusion (47%). The mean change in aPTT and INR was comparable in both the groups ($p>0.05$).
Conclusions: Analysis of appropriateness of transfusion according to BSH guidelines shows a high rate of irrational transfusions in Indian subjects. Further studies including large sample size are needed in this context.

Keywords: Appropriate, Fresh frozen plasma, Inappropriate, Packed red blood cell

INTRODUCTION

Blood transfusion practice is critical in management of patients undergoing surgeries. The use of red cell and fresh frozen plasma (FFP) transfusion is inevitable in intensive care units (ICU). Inappropriate usages not only cause wastage of limited resources but can also cause shortage of blood products for the needy patients which ultimately increases health care cost and also increases the risk of transfusion related complications. Most of the transfusion associated complications remain less recognized in critically ill patients. Hence there is a need to evaluate the use of these blood components especially in patients admitted in intensive care units.

Packed red blood cell transfusion is needed to correct anemia in ICU patients which is very frequent. Several studies reported that approximately one third of critically ill patients received a blood transfusion at one or more times during their stay in the ICU.[1-4]Anaemia in ICU patients is multifactorial in origin. The main etiologies described in literature are reduced red cell production,

reduced red cell survival, nutritional deficiency, deranged iron metabolism, low erythropoietin levels, abnormal red cell metabolism and function and hemodilution due to over usage of colloids and crystalloids.[5-8]

Fresh frozen plasma contains stable coagulation factors, plasma proteins such as immunoglobulins, albumin and the labile factors V and VIII and its transfusion is an effective way to correct the deficiency of multiple coagulation factors.[9,10] Coagulopathy is highly prevalent in ICU patients. An international normalized ratio (INR) of >1.5 occurs in approximately 30% of patients and is associated with increased mortality.[11] The important risk factors for coagulopathy are sepsis, liver disease, multiple transfusions and trauma etc.[11,12]

To reduce the inappropriate use of blood components, various strategies have been developed. These include guidelines and consensus conferences as well as monitoring of transfusion practice, education and audits.[13-15] Various studies depicting the appropriateness of blood transfusions have been published worldwide and they are having structured guidelines for the use of blood products relevant to their situations.[16] In our country, there is lack of sufficient data available about transfusion practices particularly in post-surgical ICU's.

With this background the present study was undertaken to evaluate the appropriateness of use of red cell and fresh-frozen plasma transfusions in post-surgical adult patients admitted in ICU according to the guidelines given by The British Society for Hematology (BSH guidelines, previously known as BCSH guidelines).[17,18]

METHODS

It was a retrospective observational study, conducted in the department of transfusion medicine at a tertiary care hospital for two years period after the approval by the institutional ethics committee during January 2016 to December 2017. A total number of 800 ICU adult patients were enrolled. Out of these 600 patients received PRBC transfusion and 200 received FFP transfusions. Patients who were pregnant or those who received plasma exchange therapy were excluded. Transfusion pattern was analyzed with respect to the number of units (PRBC/FFP) transfused, day of first transfusion, pre and post transfusion hemoglobin (for PRBC transfusion) levels and pre and post transfusion prothrombin time (PT), activated partial thromboplastin time (aPTT) and international normalized ratio (INR) levels (for FFP transfusion). The clinical status of the patient was assessed by recording the data of mechanical ventilation, central venous catheter in situ, need for dialysis. The outcome was measured in terms of mortality, presence of postoperative infections, new organ failure and length of ICU stay. A dose of 4 ml/kg for red cell transfusion and a dose of 10-15 ml/kg for fresh frozen plasma transfusion was considered as appropriate (based on BCSH guidelines on the administration of blood components, 2009). Here one unit of PRBC means a unit containing around 240-260 ml of packed red cells and one unit of FFP means a unit containing 150-170 ml of fresh frozen plasma. Transfusions were categorized into appropriate and inappropriate based on transfusion triggers used as per BSH guidelines (British Society for Hematology).[18] The data obtained from this study was analyzed by using SPSS (Statistical product and service solutions, SPSS Inc., Chicago, IL) software for Windows.

RESULTS

Results were analyzed separately by dividing the subjects in two groups; group A: packed red cell (PRBC) transfusion and group B: FFP transfusion group respectively.

Group A: packed red cell (PRBC) transfusion

Out of total six hundred, 384 were those with appropriate red cell transfusion while 216 were those with inappropriate red cell transfusion. In both the appropriate and inappropriate transfusion groups, majority were males (62.5% and 52.31% respectively). In the appropriate transfusion group, majority i.e. 167 (43.49%) underwent three blood unit of red cell transfusion while the inappropriate transfusion group, 144 (66.67%) patients received two units of red cell transfusion.

Table 1: Mean post-operative day of 1st transfusion and mean number of PRBC units transfused.

Mean values	Appropriate transfusion	Inappropriate transfusion	P value
Post-operative day of 1st transfusion	1.78±1.01	2.03±0.92	<0.05
Mean number of PRC units	3.35±0.97	2±0.59	<0.05

The mean post-operative day of 1st red cell transfusion was significantly lower ($p<0.05$) in the appropriate transfusion group and mean number of PRBC units transfused were significantly more in the appropriate transfusion group ($p<0.05$) by unpaired t test (Table 1).

Five hundred and fifteen (85%) of the total 600 patients were on mechanical ventilation. Majority (89) of them were on ventilation till day 5 post-operatively. In the appropriate transfusion group, majority 55 (15.45%) had ventilation till post-operative day 6 while majority in the inappropriate transfusion group 36 (22.93%) had ventilation till post-operative day 5. The mean duration of

mechanical ventilation in appropriate group was 7.43±4.1 days and in inappropriate group was 5.95±3.34 days. This was statistically significant with a p value of <0.05.

Sixty-one patients of the total (14.59%) had central line for 4 days post-operatively. In the appropriate transfusion group, majority 31 (12.4%) had central line till post-operative day 4 while majority in the inappropriate transfusion group 36 (21.43%) had central line till post-operative day 5. The mean duration of central line in inappropriate group was 7.7±4.17 days and in appropriate group was 5.36±3.07 days. This was statistically significant with a p value of <0.05.

On comparison of the mean increase in the post-transfusion hemoglobin, SaO_2 and PaO_2 between the pre-transfusion and post-transfusion group it was found that the mean increase in the hemoglobin and SaO_2 in the appropriate transfusion group was significantly higher (p<0.05). The mean change in PaO_2 were comparable in both the groups (p>0.05) (Table 7).

Table 2: Mortality and ICU stay (PRC transfused patients).

Parameters assessed	Appropriate transfusion (%)	Inappropriate transfusion (%)	All patients (%)
7-day mortality	36 (9.3)	16 (7.4)	52 (8.6)
30-day mortality	48 (12.5)	6 (2.7)	54 (9)
ICU stay (days)	Median: 9 (range=1-29)	Median: 7 (range =2-26)	Median: 8 (range =1-29)
	Mean: 10.08±4.83	Mean: 7.87±3.68	Mean: 9.28±4.58

Table 3: Association between mortality and appropriateness of transfusion (PRBC transfusion).

Parameters assessed	Appropriate transfusion (%)	Inappropriate transfusion (%)	P value
Mortality present	84	22	<0.05
Mortality absent	300	194	
Total	384	216	

Table 4: Association between post-operative infections and appropriateness of transfusion (PRBC transfusion).

Parameters assessed	Appropriate transfusion (%)	Inappropriate transfusion (%)	P value
Post-operative infections present	136	33	<0.05
Post-operative infections absent	248	183	
Total	384	216	

Table 5: Association between new organ failure and appropriateness of transfusion (PRBC transfusion).

Parameter assessed	Appropriate transfusion (%)	Inappropriate transfusion (%)	P value
New organ failure present	78	22	<0.05
New organ failure absent	306	194	
Total	384	216	

Table 6: Pre-transfusion and post-transfusion parameters (PRBC transfusion).

Parameters assessed	Pre-transfusion value			Post-transfusion value			P value
	Appropriate transfusion	Inappropriate transfusion	Total	Appropriate transfusion	Inappropriate transfusion	Total	
Hb (gm/dl)	6.69±1.11	8.91±0.90	7.49±1.49	7.51±1.19	9.47±0.93	8.21±1.45	<0.05
SaO_2 (%)	88.96±2.53	92.08±3.16	90.09±3.15	95.15±2.02	94.66±1.95	94.97±2.01	<0.05
PaO_2 (mmHg)	76.77±6.13	87.19±7.47	80.53±8.31	84.65±7.17	96.76±8.94	89.01±9.76	<0.05

Of the total patients, fifty-two patients had 7-day mortality while 54 patients had 30-day mortality. Out of these, majority were from the appropriate transfusion group. The mean or median ICU stay was also more in the appropriate transfusion group. The mean ICU stay in the inappropriate transfusion group was found to be significantly lower (p<0.05) by unpaired t test analysis as compared to that in the appropriate transfusion group (Table 2). There was significant association found between the high mortality and appropriateness of blood transfusion (p<0.05) (Table 3).

Total 169 patients suffered from post-operative infections (sepsis, wound infection, meningitis peritonitis surgical

site, infection, acute kidney injury, wound abscess, URTI). Out of these, 39.05% suffered from sepsis. In the appropriate and inappropriate transfusion groups, 41.91% and 27.27% respectively suffered from sepsis.

There was significant association found between the high occurrence of post-operative infections and appropriateness of blood transfusion ($p<0.05$) (Table 4).

100 patients reported to have new organ failure (renal failure, acute MI, ARDS, liver failure, stroke) in the post-operative period during their stay in the ICU. Out of these, majority (51%) had renal failure. 44 (51.28%) and 11 (50%) patients respectively from appropriate and inappropriate transfusion groups suffered from renal failure, the most common organ failure. There was significant association found between the high occurrence of new organ failure and appropriateness of blood transfusion ($p<0.05$) (Table 5).

Group B: fresh frozen plasma (FFP) transfusion

A total of 200 patients who had received FFP transfusion were included in the study. Out of these, 137 were those with appropriate transfusion while 63 were those with inappropriate transfusion. In both the appropriate and inappropriate transfusion groups, majority were males (64.23% and 55.55% respectively). Of those who underwent transfusion intra-operatively (24.82%) underwent transfusion with two FFP unit in the appropriate transfusion group and 28.57% patients with two FFP unit in the inappropriate transfusion group as well. Majority with (36.5%) underwent first post-operative FFP transfusion on day 1 In the appropriate transfusion group and majority with 34.92% patients underwent first post-operative transfusion on day 3 In the inappropriate transfusion group respectively.

Majority of the overall total patients underwent two units of post-operative FFP transfusion (47%). In the appropriate transfusion group, majority (48.18%) underwent two FFP unit of post-operative transfusion and majority (44.44%) patients underwent two units of post-operative FFP transfusion with in the inappropriate transfusion group respectively .The mean post-operative day of 1st transfusion was significantly lower ($p<0.05$) in the appropriate transfusion group but the mean number of FFP units transfused were comparable in the appropriate and inappropriate transfusion groups ($p>0.05$) by unpaired t test (Table 7).

Table 7: Mean post-operative day of 1st transfusion and mean number of FFP units transfused.

Mean values	Appropriate transfusion	Inappropriate transfusion	P value
Post-operative day of 1st transfusion	2.27±1.29	3.23±1.1	<0.05
Mean number of FFP units	2.54±0.77	2.41±0.79	0.43

Table 8: Comparison between the mean decrease of coagulation parameters in the post-transfusion parameters (FFP transfusion).

Post-operative mean decrease in values	Appropriate transfusion group	Inappropriate transfusion group	P value
PT	5.08±0.02	4.11±0.09	<0.05
aPTT	4.93±1.2	4.92±1.1	0.85
PT-INR	0.67±0.05	0.26±0.02	0.18

Table 9: ICU stay (FFP transfused patients).

Parameter assessed	Appropriate transfusion (%)	Inappropriate transfusion (%)	All patients (%)
ICU stay (days)	Median: 8 (range = 5-17)	Median: 8 (range = 5-15)	Median: 8 (range = 5-17)
	Mean: 9.36±2.6	Mean: 8.84±2.54	Mean: 9.14±2.65

Table 10: Association between post-operative infections and appropriateness of FFP transfusion.

Parameter assessed	Appropriate transfusion (%)	Inappropriate transfusion (%)	P value
Post-operative infections present	35	17	0.86
Post-operative infections absent	102	46	
Total	384	216	

There was a statistically significant decrease in the PT, aPTT and the INR values after transfusion ($p<0.05$) overall as well as when analyzed in sets of patients with appropriate as well as inappropriate transfusion (Table 8).

On comparison on the mean decrease in the post-transfusion PT, aPTT and INR values between the pre-transfusion and post-transfusion group, it was found that the mean decrease in the PT in the appropriate

transfusion group was significantly higher ($p<0.05$). The mean change in aPTT and INR was comparable in both the groups ($p>0.05$) (Table 8).

The mean ICU stay in the inappropriate transfusion group was found to be significantly lower ($p<0.05$ by unpaired t test). The median in both the sub-groups were same (8 days) (Table 9).

A total of 52 patients (26%) suffered from post-operative infections (sepsis, bronchopneumonia, wound infection, mediastinitis, meningitis, peritonitis, surgical site infection, cellulitis, colitis). Out of these, 48.08% suffered from sepsis. In the appropriate and inappropriate transfusion groups, 51.43% and 41.18% respectively suffered from sepsis. There was no significant association found between the high occurrence of post-operative infections and appropriateness of FFP transfusion ($p=0.86$) (Table 10).

Thirty-one (15.5%) patients reported to have new organ failure (renal failure, acute MI, atelectasis, ARDS) in the post-operative period. Out of these, majority (35.48%) had renal failure [6 (30%)] and [5 (45.45%)] patients respectively from appropriate and inappropriate transfusion groups suffered from renal failure, the most common organ failure. There was no significant association found between the high occurrence of new organ failure and appropriateness of FFP transfusion ($p>0.05$).

Correlation between number of FFP units transfused and the number of ICU days was done by using Pearson test, it was found to be 0.05, indicating negligible correlation. This correlation finding was statistically insignificant ($p=0.47$).

DISCUSSION

PRBC transfusion

In our study we found that out of total six hundred, 384 were those with appropriate red cell transfusion while 216 were those with inappropriate red cell transfusion. In the appropriate transfusion group, majority i.e. 167 (43.49%) underwent three blood unit of red cell transfusion while the inappropriate transfusion group, 144 (66.67%) patients received two units of red cell transfusion. Those patients who underwent mechanical ventilation, the mean duration of mechanical ventilation in appropriate group was significantly more (7.43±4.1 days versus 5.95±3.34 days). The mean duration of central line in inappropriate group was more (7.7±4.17 days versus 5.36±3.07 days).

On comparison of the mean increase in the post-transfusion hemoglobin, SaO_2 and PaO_2 between the pre-transfusion and post-transfusion group it was found that the mean increase in the hemoglobin and SaO_2 in the appropriate transfusion group was significantly higher ($p<0.05$) while the mean change in PaO_2 were comparable in both the groups ($p>0.05$).

We also found the significant association of mean ICU stay as well as 7-day mortality which were more in the appropriate transfusion group. There was significant association found between the high occurrence of post-operative infections and appropriateness of blood transfusion. The study results are comparable with other studies where the mortality rate increased as the units of transfusion increased.[19-21] These studies also showed that the increased number of transfused units are associated with increased ICU stay which is similar to the present study.

There was significant association found between the high occurrence of new organ failure and appropriateness of blood transfusion ($p<0.05$). The significant mild Correlation between Number of PRBC units transfused and the number of ICU days was also found.

So, from our findings it is clear that a greater number of PRBC transfusion are associated with poor morbidity and outcomes. It also suggests that restrictive transfusion strategy in non-hemorrhaging critically ill patients should be opted. The study conducted by Netzer et al also supported the restrictive use of transfusion in ICU patients.[22] We tried to find out studies carried out on our population regarding this study, but could not found any comparable study.

FFP transfusion

Out of two hundred patients, 137 were those with appropriate transfusion while 63 were those with inappropriate transfusion.

In our study we found that same number of FFP units were transfused to the patients during intraoperative and post operative period as well when we compared between appropriate and inappropriate transfusion group. The appropriate group received 1st transfusion early.

On comparison on the mean decrease in the post-transfusion PT, aPTT and INR values between the pre-transfusion and post-transfusion group, it was found that the mean decrease in the PT in the appropriate transfusion group was significantly higher ($p<0.05$). The mean change in aPTT and INR was comparable in both the groups ($p>0.05$).

The mean ICU stay in the inappropriate transfusion group was found to be significantly lower. There was no significant association found between the high occurrence of post-operative infections and appropriateness of FFP transfusion. There was no significant association found between the high occurrence of new organ failure and appropriateness of FFP transfusion. No correlation between number of FFP units transfused and the number of ICU days was found.

The data suggest that there was significant decrease in PT value in the appropriate transfusion group when compared with another group. However, length of stay in ICU and associated sepsis and new organ failure were not showing any significant association between these two groups.

This has been advised that every single FFP unit should be transfused as an independent clinical decision and the relative risks and benefits to the patient should also be taken into account. Many studies have shown greater prevalence of inadequate use of FFP. Comparable data have been reported at national level.[20] The common areas of misuse may include volume replacement, mildly elevated PT, APTT in the absence of bleeding, hypoproteinemia, post-operative wound healing, prophylactic transfusion in dengue and other single- or double-unit transfusions which were subtherapeutic.[23]

Present study was tertiary care hospital based involving only smaller number of subjects so we require more studies regarding this subject in our country.

CONCLUSION

Our study showed that blood transfusion strategies using BSH guidelines used more liberal transfusion approach in stable critically ill patients and it did not appear to be associated with a significant clinical benefit. Analysis of appropriateness of transfusion according to BSH guidelines revealed a high rate of irrational transfusions in Indian subjects. Hence there is a need to conduct such type of study on large sample and different parts of our country so that universal strategies and guidelines can be formed based on clinical as well as laboratory parameters for the use of blood components in post-operative critically ill patients.

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