ISSN: 0976-3031

Available Online at http://www.recentscientific.com

CODEN: IJRSFP (USA)

International Journal of Recent Scientific Research
Vol. 10, Issue, 01(C), pp. 30375-30378, January, 2019

International Journal of Recent Scientific Research

DOI: 10.24327/IJRSR

Research Article

THE THERAPEUTIC RESPONSE TO LOW DOSE PLATELET TRANSFUSION IN HEMATO-ONCOLOGICAL PATIENTS

Abhijit Mandal[1]., Samir Kumar Roy[2] and Kusumita Mandal[3]*

[1]Department of Health & Family Welfare, Swasthya Bhawan, Salt Lake, Kolkata
[2]Department of Cardiology, N R S Medical College, Kolkata
[3]Department of Immunohematology & Blood Transfusion, Medical College, Kolkata

DOI: http://dx.doi.org/10.24327/ijrsr.2019.1001.3046

ARTICLE INFO

Article History:

Received 4th October, 2018
Received in revised form 25th October, 2018
Accepted 18th December, 2018
Published online 28th January, 2019

Key Words:

Thrombocytopenia, Hemato-oncological Patients, CCI (corrected count increment), PPR (percentage platelet recovery)

ABSTRACT

Introduction: The amount of platelets considered a therapeutic dose remains controversial and undecided. The multiple studies show that a lower platelet dose for prophylactic transfusions was not inferior to the standard dose.[9] **Method:** 61 patients with haemato-oncological patients with severe thrombocytopenia underwent platelet transfusion with group specific single donor apheresis platelets of low dose. We define 1.1 to 1.9 × 10^{11} platelets/ transfusion as low dose. The successful platelet transfusion can be assessed by calculating corrected count Increment (CCI) and percentage platelet recovery (PPR) at 1 hour and 24 hours post transfusion which indicate the functional platelets in circulation. **Results:** The mean ± SD & range of t CCI at 1 hour were 12265.28 ± 3531.09 (SD) & 3916 to 21677 and after 24 hours 8310.43 ± 2698.73 (SD) & 1350 to 16722 respectively. In the CCI at 24 hours it was observe, d that there were 11.48% (7) cases having the CCI below 4500 and 88.52% (54) cases were belonged to the groups of 4500 & above. Only 16.39% (10) cases were having PPR of below 30% and 83.61% (51) cases had the PPR of 30% & above at 1 hour. PPR at 24 hours showed that only 16.39% (10) cases were having PPR of below 20% and 83.61% (51) cases had the PPR of 21% & above. **Conclusion:** Low dose platelet transfusion (1.1-1.9× 10^{11} platelets / dose),is good enough to attain therapeutic response in terms of CCI and PPR. Thus both hazards and cost related to transfusion can be minimized.

INTRODUCTION

Patients with severe thrombocytopenia presumed to have increased risk of bleeding. Platelet transfusions to this patients may be given either prophylactically to reduce the risk of bleeding in the absence of clinical haemorrhage (prophylactic transfusions), or to control active bleeding when present (therapeutic transfusions). The amount of platelets considered a therapeutic dose remains controversial and undecided.[1]The question of what the optimal platelet dose is has been approached in several ways. A mathematical model was used to calculate the smallest number of platelets that would need to be transfused to a patient to achieve the desired target level who reached the transfusion threshold.[2] This analysis argued for the use of small therapeutic doses administered more frequently. The use of larger units in a clinical study resulted in longer inter-transfusion intervals, although this temporal increase was smaller than the increase in the number of platelets transfused.[3] Themulticentre, prospective randomized controlled trial show that a lower platelet dose for prophylactic transfusions was not inferior to the standard dose.[4]

The successful platelet transfusion can be assessed by calculating corrected count Increment (CCI) and percentage recovery (PR) at 1 hour and 24 hours post transfusion which indicate the functional platelets in circulation. If the CCI at 1 hour and 24 hours are less than 7500/µl/m^2 and 4500/ µl/m^2 and PPR at 1 hour and 24 hours are less than 30% and 20% respectively on two consecutive occasions it indicates refractoriness.[5]

Background

As until recently there have been very few prospective, randomized clinical trial (RCT) data globally for evaluating the relative effects of different platelet regimens or platelet doses on clinical outcomes and little data available in India about the response to low dose platelet transfusions in haemato-oncological patients, it is required to perform the study not only to optimize the dose of platelet transfusions but to manage the

Corresponding author:* **Kusumita Mandal
Department of Immunohematology & Blood Transfusion, Medical College, Kolkata

platelet inventory efficiently and cost-effectively which is also a challenge in our country.

Slichter *et al*.[6] conducted a RCT of prophylactic platelet transfusions to determine the effects of the dose of platelets on clinical signs of bleeding, conclude that the dose of platelets transfused has no significant effect on the incidence of bleeding in patients with hypoproliferative thrombocytopenia and platelet counts no greater than 10×10^9/l.

Paolo Rebulla *et al*.[7] revealed that the risk of major bleeding during induction chemotherapy in adolescents and adults with acute myeloid leukemia was similar with transfusion threshold of 20000 per µl and 10000 per µl. Use of lower threshold reduced platelet transfusion by 21.5 percent.

A double-blind randomized control trial (RCT) comparing standard and low dose strategies for transfusion of platelets (Stop) to patients with thrombocytopenia by Nancy *et al*.[4] found noninferior outcome to compare low-dose and standard-dose prophylactic platelet transfusions. WHO bleeding grade 2 or higher was 49.2% (30/61) in the standard-dose arm and 51.7% (30/58) in the low-dose arm (relative risk [RR]–1.52; 95% confidence interval [CI], 0.737-1.502).

'The impact of platelet transfusion characteristics on post-transfusion platelet increments and clinical bleeding in patients with hypoproliferative thrombocytopenia' by Darrell J. Triulzi *et al*.[8] analyzed for the platelet increment were also analyzed for four hour CCI. The overall test for an effect of dose was not statistically significant (p = 0.13), and there was no significant difference in the four hour CCI for low-dose versus the medium-dose arm. Escourt L J *et al*.[9]with the objective to determine whether different doses of prophylactic platelet transfusions effect their efficacy and safety in preventing bleeding in people with malignant hematological disorders or undergoing HSCT that compared different platelet component doses (low 1.1×10^{11}/ m^2 ± 25%, standard dose 2.2×10^{11} / m^2 ± 25%, high dose 4.4×10^{11} / m^2 ± 25%). There were no difference in number of participants with clinically significant episode between low-dose and standard-dose group (four studies; 1170 participants; risk ratio (RR) 1.04, 95% confidence interval (CI) 0.95 to 1.13; moderate quality evidence); low-dose and high-dose groups (one study; 849 participants; RR 1.02,95% CI 0.93 to 1.11; moderate quality evidence); or high-dose and standard-dose groups (two studies; 951 participants; RR 1.02, 95% CI 0.51to o.17; low quality evidence).

MATRIAL & METHODS

This prospective and observational study was conducted in the department of Immunohaematology & Blood Transfusion (IHBT) and Institute of Haematology & Transfusion Medicine (IHTM) Medical College Hospital, Kolkata for the period of one and half years (January 2014 to June 2015). The study population was all haemato-oncological patients with severe thrombocytopenia having platelet transfusion of Medical College Hospital, Kolkata.

The inclusion criteria were all haemato-oncological patients of age above 2 years with severe thrombocytopenia (platelet count less than 20000/ µl).

The exclusion criteria were the patients with secondary causes of thrombocytopenia like infection, fever, sepsis, DIC, hypersplenism, hepatitis, and drugs like NSAIDS, Cyclophosphamide, Amphotericin B etc.

The parameters used in the study were platelet count of the product bag, pre-transfusion platelet count of the patient, post-transfusion platelet count at 1 hour & 24 hours done with automated cell counter (CELL-TECH, made in EU) and Corrected Count Increment (CCI) & post-transfusion Percentage Platelet Recovery (PPR) at 1 hour & 24 hours. Patients with platelet count below 20000/ µl.transfused with group specific single donor apheresis platelets. Low dose prepared by dividing the product bag into two halves. In our study we define 1.1 to 1.9×10^{11} platelets/ transfusion as low dose.

After taking a valid consent form the patients and after getting clearance from the Ethical Committee of the institution, a brief clinical history & physical examination including age, sex, height and weight were recorded. The detailed history of previous platelet and red cell transfusions were also taken as they might have developed immune-refractoriness due to multiple transfusions.

RESULTS

All the 61 patients, 35(57.38%) were male and 26 (42.62%) were female, under study were transfused with group specific single donor apheresis platelets of low dose prepared by dividing the product bag into two halves. In the study the minimum Age of the patient was 9 years and maximum age was 73 years. The mean age was found to be 36.52 ± 16.78 (SD) years.

Table 1 Distribution of cases according to their gender versus diagnosis

Diagnosis	Female		Male		Total	
	No.	%	No.	%	No.	%
AA	7	26.92	8	22.86	15	24.59
ALL	4	15.38	10	28.57	14	22.95
AML	13	50.00	13	37.14	26	42.62
BURKITS LYMPHOMA	--	--	1	2.86	1	1.64
MDS	--	--	2	5.71	2	3.28
MM	--	--	1	2.86	1	1.64
PRIMARY AMYLOIDOSIS	1	3.85	--	--	1	1.64
Thrombocytopenia	1	3.85	--	--	1	1.64
Total	26	100.00	35	100.00	61	100.00

Study populations were distributed according to their gender and diagnosis. Among 61 cases 15 (24.59%) had AA, 14 (22.95%) had ALL, 26 (42.62%) had AML, 1(1.64%) had BURKITS LYMPHOMA, 2 (3.28%) had MDS, 1 (1.64%) had MM, 1(1.64%) had PRIMARY AMYLOIDOSIS and 1(1.64%) had THROMBOCYTOPENIA.

Table 2 Corrected Counted Increment (CCI) at 1 Hour

Corrected count increment	No.	%
<7500	8	13.11
7500-9999	1	1.64
10000-12499	21	34.43
12500-14999	21	34.43
>=15000	10	16.39
Total	61	100.00

Table 3 Corrected Count Increment (CCI) at 24 Hours

Corrected count increment	No.	%
<4500	7	11.48
4500-7499	7	11.48
7500-9999	34	55.73
10000-12499	10	16.39
12500-14999	2	3.28
>=15000	1	1.64
Total	61	100.00

Table 4 PPR at 1 hour

PPR	No.	%
<30	10	16.39
30-40	43	70.49
41-50	8	13.12
Total	61	100.00

Table 5 PPR at 24 hours

%PPR	No.	%
<=20	10	16.39
21-30	47	77.05
31-40	4	6.56
Total	61	100.00

In our study platelet transfusions were given on the threshold ranging from 4000/ µL to 14000/ µL and the mean value of transfusion threshold was 8737.70 ± 2007.50 (SD) per µL

In our study low- dose platelet (LDP) for transfusion was defined as the dose having platelet count ranging from 1.1 to 1.9×10^{11}/ product bag. Here we prepared the desired dose from single donor apheresis platelet (SDP) product by dividing it into two halves and were given to all 61 patients of the study group. The mean ± SD of low-dose platelet in platelet bag were $(1.69 \pm 0.15) \times 10^{11}$& range was $(1.2\text{-}1.9) \times 10^{11}$

The mean ± SD & range of corrected count increment (CCI) at 1 hour were 12265.28 ± 3531.09 (SD) & 3916 to 21677 and after 24 hours 8310.43 ± 2698.73 (SD) & 1350 to 16722 respectively

In the CCI at 24 hours it was observed that there were 11.48% (7) cases having the CCI below 4500 and 88.52% (54) cases were belonged to the groups of 4500 & above. The post-transfusion percentage platelet count (PPR) at 1 hour showed that only 16.39% (10) cases were having PPR of below 30% and 83.61% (51) cases had the PPR of 30% & above.

The post-transfusion percentage platelet count (PPR) at 24 hours showed that only 16.39% (10) cases were having PPR of below 20% and 83.61% (51) cases had the PPR of 21% & above.

DISCUSSION

In this prospective and observational study we found that the mean post-transfusion platelet increment was 13557.37 ± 5302.59 (SD) / µl, 1 hour after transfusion of our low-dose platelet (LDP) which contains a mean platelet count of $1.69 \pm 0.15 \times 10^{11}$ (SD) / dose with range of 1.2 to 1.9×10^{11} / dose administered in random order in 61 haemato-oncological patients. In a study Klumpp TR *et al*.[10] reported that the mean post-transfusion platelet increment at 1 hour with low dose platelet (LDP) was 17010 / µl against the mean dose of LDP of 3.1×10^{11} / dose and range was $2.3\text{-}3.5 \times 10^{11}$ / dose which was almost twice the dose of our study . The mean 4 hour absolute increment of platelet observed 13519 / µl with low dose platelet transfusion strategy and also was as effective as the other dose strategies for bleeding prophylaxis as shown in analysis in well known PLADO study[14] and slichler *et al*.[15] So it logically follows that the higher mean increments observed with platelets will be similarly effective.

The post-transfusion mean absolute increment of platelet count after 24 hours was 9049.18 ± 4279.51(SD) / µl. In one study conducted by Slichter *et al*.[11] the mean 18-24 hour platelet increment was 12000 (± 15) / µl in response to a high dose platelet transfusion strategy and in another study by Shamee Shastry *et al*.[12]the post-transfusion mean platelet increment after 24 hours was found to be 17789/ µl against transfusion of single donor apheresis platelets (SDP) units of higher doses to each patient. In both the cases, the transfusion dose of platelets administered were higher than the dose used in our study.

In our study we observed the mean 1-hour corrected count increment (CCI) was 12265.28 ± 3531.09(SD) and range 3916 to 21677. The mean 24-hour CCI was 8310.43 ± 2698.73 (SD) and range 1350 to 16722. According to Bishop *et al*.[13] the effectiveness of platelet transfusion at 1 hour and 24 hours are strictly correlated and CCI at 24 hours is approximately 64% of CCI at 1 hour. In our study, visibly the difference seen (67%) is more than the expected value but on statistical test (paired t test) it was found not significant (p = 1.089) in case of CCI at 1 hour and 24 hours.

We evaluated 1-hour CCI values and found 86.89% (53) cases had adequate therapeutic response in view of successful transfusion as they all were having CCI values more than 7500, 85.25% (52) cases had CCI values 10,000 and above and only 13.11% (8) cases were seen under unsuccessful transfusion(1-hour CCI < 7500). We also evaluated the 24-hour CCI values and found 88.52% (54) cases having CCI values 4500 & above were under successful transfusion group and only 11. 48% (7) cases belonged to unsuccessful group as they were having 24-hour CCI value below 4500.

We observed the rate of successful transfusion is much higher in our study probably because we excluded cases having non-immune causes of platelet refractoriness like fever, sepsis, infection, bleeding, hypersplenism & drug like NSAIDs, Amphotericin B etc. which constitute a major causes refractoriness and are significantly associated with decreased CCI.[16] In a study by Pereira *et al*.[17]reported only 17% of patients were refractory and Hacene Brouk *et al*.[18] found only 10.26% patients with antibodies against platelet and consistent with our study. Whereas, in India N Agarwal *et al*.[19] found 37.35% patients and Meenu Bajpai *et al*.[20] observed 71.4% patients with platelet reactive antibodies in multitransfused patients. In another prospective study by H.A. Doughty *et al*.[21] 44% of platelet transfusions failed to produce satisfactory response and Kifefel *et al*.[22] had observed platelet reactive antibodies in 44.8% of cases. A. Ishida *et al*.[23] reported that the mean platelate count at 16-hour & percentage of CCI for all transfusions were 6161.1 ± 7775.2 and 42.1% they concluded that alloimmunization is not a major factor associated with poor response to platelet transfusions also support the result of our study.

We also evaluate the 1 hour post-transfusion percentage platelet recovery (PPR), the mean value 32.6 ± 8.93 %(SD) and 83.6% cases with PPR 30% and above represents

successful transfusion in majority of cases. Study by Delaflor-weiss E *et al*.[24]showed that an average 1 hour PPR of approximately 66%.

The 24 hour post-transfusion percentage platelet recovery (PPR), the mean value 21.5 ± 6.75 %(SD) and 83.61% cases with PPR 20% and above represents successful transfusion in majority of cases.

CONCLUSION

In the present study we observed if the dosing of platelet can be appropriated and standardized in the institutional level to low dose platelet transfusion (1.1-1.9× 10^{11} platelets / dose),is good enough to attain therapeutic response in terms of CCI and PPR.thus both cost related transfusion and transfusion related hazards can be minimized.

References

1. AABB, Technical Manual (18th edition) 2014; 510.
2. Hersh JK, Hom EG, Brecher ME. Mathematical modelling of platelet survival with implications for optimal transfusion practice in the chronically platelet transfusion-dependent patient. Transfusion 1998; 39:637-644.
3. Norol F, Bierling P, Roudot-Thoraval F, *et al*. Platelet transfusion: A dose response study. Blood 1998; 92: 1448-53.
4. Heddle NM, Cook RJ, Tinmouth A, Kouroukis CT, Hervig T, Klapper E, Brandwein JM, Szczepiorkowski ZM, AuBuchon JP, Barty RL, Lee KA; SToP Study Investigators of the BEST Collaborative. A randomized controlled trial comparing standard- and low-dose strategies for transfusion of platelets (SToP) to patients with thrombocytopenia. Blood. 2009 Feb 12; 113(7):1564-73.
5. Saran RK. Transfusion medicine technical manual.DGHS. 2nd ed. India: Ministry of Health and Family Welfare;2003.pp. 341-60.
6. Sherrill J. Slichter, M.D., *et al* Dose of Prophylactic Platelet Transfusionsand Prevention of Hemorrhage (Abstract).Thenew England journal of medicine 2010,362;7.
7. Rebulla P, Finazzi G, Marangoni F, Avvisati G, Gugliotta L, Tognoni G, Barbui T, Mandelli F, Sirchia G. The threshold for prophylactic platelet transfusions in adults with acute myeloid leukemia: N Engl J Med. 1997 Dec 25; 337(26):1870-5.
8. Darrell J. Triulzi *et al*. The impact of platelet transfusion characteristics on post-transfusion platelet increments and clinical bleeding in patients with hypoproliferative thrombocytopenia. Blood.2012 Jun 7; 119(23):5553 - 55562
9. Escourt L J *et al*. Different doses of prophylactic platelet transfusion for preventing bleeding in people with hematological disorders after myelosuppressive chemotherapy or stem cell transplantation. Cochrahe databadse syst rev. 2015 oct 27; 10.
10. Klumpp TR *et al*. Transfusion 1999; 39:674-81.
11. Slichter SJ, Davis K, Enright H, Brain H, Gernsheimer T, Kao K, *et al*. Factors affecting post-transfusion platelet increments, platelet refractoriness, and platelet transfusion intervals in thrombocytopenic patients. Blood 2005; 105:4106-14.
12. Shamee Shastry, Rajenra Chaudhary. clinical factors influencing corrected count increment. Transfusion and Apheresir Science.2012**.**
13. Bishop JF, Matthew JP, Yuen K, McGrath K, Wolf MM, szer J. The definition of refractoriness to platelet transfusions. Transfus Med 1992; 2:35-41.32.
14. Slicher SJ, Kaufman RM, Assman SF, *et al*. Dose of prophylactic platelet transfusion and prevention of haemorrhage. N Engl J Med 2010.
15. Slichter SJ, Harker LA. Thrombocytopenia: mechanisms and management of defects in platelet production. Clin Haematol. 1978; 7:523-539.
16. Bock M, Muggventhaler KH, Schmidt U, Heim MU. Influence of antibiotics on post-transfusion platelet increment refractoriness. Ttrnsfusion 1996; 93:220-4.
17. Pereira J *et al*. Revista Medica De Chile 1997, 125(11):1305-1312.
18. Hence Brouk *et al*. Transfusion and Apheresis Science June 2015, vol.52 (3); 295-299.
19. N Agarwal *et al*. Asian J Transfus Sci.2014 Jul-Dec; 8(2): 126 -127.
20. Meenu Bajpai *et al*. Platel *et al* loimmunization in multitransfused patients with haemato-oncologocal disorders. Natl Med J India 2005; 18:134-6.
21. Doughty HA, Murphy MF, Metcalfe P, Rohatiner AZS, Lister TA, waters AH. Relative importance of immune and non-immune causes of platelet refractoriness. Vox sang 1994; 66:200-5.
22. Kiefel V, Konig C, Kroll H, Santos S. Platel*et al* loantibodies in transfused patients. Transfusion 2001; 41:762-5.
23. A. Ishida *et al*. clinical factors influencing post-transfusion platelet increment in patients undergoing hematopoietic progenitor cell transplantation'-a prospective analysis. Transfusion. 1998; sept 38(9): 839-847.
24. Deleflor-Weiss E, Mintz PD. The evaluation and management of platelet refractoriness and alloimmunization. Trans Med Rev 2000; 14:180-96.

How to cite this article:

Kusumita. 2019, The Therapeutic Response to Low Dose Platelet Transfusion in Hemato-Oncological Patients. *Int J Recent Sci Res.* 10(01), pp. 30375-30378. DOI: http://dx.doi.org/10.24327/ijrsr.2019.1001.3046

****