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An Open-labelled Randomized Cross-Over Study of the Effect of Electromechanical Pumps Versus Conventional Gravity Flow on Platelet Transfusion in Adult Oncology Patients

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Abstract

Background: Only few data are available regarding the effect of method of platelet transfusion on the platelet increment. Although, administering platelets either via a free flowing gravity or electromechanical pump is a common practice, there are no randomized trials addressing differences between these techniques.

Objectives: Our study is aimed to determine whether infusion methods influence the platelet increment.

Methods: We studied the effect of three different electromechanical pumps that are used routinely for transfusion at our hospital; the Graseby 3000, Imed Gemini PC-1, and the Baxter Colleague in comparison to the free-flow gravity method. Between January 2007 and January 2011, we prospectively randomised 35 patients totalling 171 episodes of platelet transfusion. Most of the patients received platelets by four different techniques. Patients with factors such as infection, coagulopathy, platelet or HLA antibodies that may influence platelet recovery were excluded.

Results: Baxter Colleague pump method was associated with the highest platelet increment 1 hour after transfusion (p=0.03). This effect vanished after 24 hours. The Gemini and Graseby pumps were similar in comparison to gravity-flow method.

Conclusion: None of the different infusion pumps were inferior to the gravity flow method. Further studies to confirm these findings are warranted.

Keywords: Platelet transfusion; Electromechanical pump; Gravity method; Platelet-increment

Introduction

Platelet transfusion is a common practice at the Launceston General Hospital (LGH) and many centres in Australia as well as all over the world. This practice allows administering platelets via either a free flowing gravity line or an electromechanical pump [1,2]. There are few centres that employ an electromechanical pump during platelet transfusion as a routine practice [2,3].

While administration of platelets via a pump offers a well-controlled infusion rate, accurate volume measurements and an alarm system for monitoring the infusion, nevertheless, in theory, there is a concern regarding potential damage to the transfused platelets [4-7].

There are three types of pumps that are available on the haematology ward at the LGH which are used for both red cell and platelet transfusion; the Graseby 3000 (Watford, Herts, UK), Imed Gemini PC-1 (San Diego, CA, USA), and the Baxter Colleague (Oklahoma, USA) pump.

Furthermore, there are no available data regarding assessment of different methods of platelet transfusion in adult populations comparing the effect of conventional gravity flow transfusion with these three common electromechanical pumps on platelet recovery post transfusion.

This study examined whether any of the above mentioned infusion method influences the platelet increment at 1 and 24 hours after the infusion. Hence this will help in assessing different techniques for administration of platelets in adult population.

Design and Methods

Design overview

This is an open-labelled randomized study conducted between January 2007 and January 2011 at the Launceston General Hospital (LGH), a tertiary referral centre for Northern Tasmania, Australia. The study was approved by the Tasmania Health and Medical Human research, Ethics Committee (EC00337). The study was registered in the Australia and New Zealand clinical trial registry under ACTRN #12609000597291. Web address of the trial: http://www.ANZCTR.org.au/ACTRN12609000597291.aspx as well as in the World Health Organization (WHO) website under http://apps.who.int/trialsearch/trial.aspx?trialid=ACTRN12609000597291. Informed consent was obtained from all patients in accordance with the Code of Ethics.

The study was designed to evaluate the influence of electromechanical pumps versus gravity flow on post transfusion platelet increment. Four methods were assigned for platelet transfusion using a 4 pack randomization key chart. These methods are: Free flowing gravity line, Graseby 3000 (Watford, Herts, UK), Gemini PC-1

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(San Diego, CA, USA), and the Baxter Colleague (Oklahoma, USA). For patients who needed further platelet transfusions, a randomisation for the remaining three methods took place each time a transfusion was required.

Objectives

The primary objective of this study was to evaluate the influence of the three different electromechanical pumps compared with gravity flow infusion on post transfusion platelet increments one and 24 hours after the transfusion. Secondary objectives were to determine the most efficient procedure for the administration of platelets and to assess whether the method of transfusion plays role in maintaining the quantity of the platelet increment.

Participants

At the LGH Haematology and Oncology ward, the treating team identified potential candidates above the age of 18 with thrombocytopenia most likely secondary to the underlying haematological disorder or secondary to the treatment received. The patient`s informatied consent was obtained prior to enrolment. Exclusion criteria included: Infection or sepsis with a temperature>38.5°C; coagulopathy or Disseminated Intravascular Coagulopathy (DIC); hypersplenism and patients who had platelet refractoriness e.g. platelet antibody or human leucocyte antigen (HLA) antibody or immune thrombocytopenia.

Thirty-five patients were included in the study totalling 171 episodes of platelet transfusion. Most of the patients received multiple platelet transfusions. Platelet transfusion was indicated primarily for patients with a platelet count of less than 20/nL as a baseline.

Randomization

Following recruitment, a random allocation sequence was generated by the researcher using 4 cards with each representing a different transfusion method respectively as following: 1; Baxter Colleague pump, 2; Gemini PC-1 pump, 3; Graseby 3000 pump, and 4; Gravity flow. Based on this a randomization key chart was provided. Randomisation was carried out by the nurse who was transfusing the platelets at the time. Participants were asked to select one card from the four offered to them and thus assigned the transfusion method according to the randomization key chart. The patient was unable to see the randomisation symbol. Once a card had been selected it was set aside so subsequent transfusions for the same patient involved a selection of one of the remaining three and so on in order to ensure an equal frequency of each of the different transfusion methods and minimise the effect of random selection of platelet transfusion method on the overall outcome

Procedure and platelet increment measurement

Patients enrolled into the study were assigned a unique identification (ID) numbers and patients' registration forms were filed accordingly and saved in a password protected folder. Clinical trial patient stickers were attached on the medical history by researcher and the medical officer notified the Pathology Laboratory of the patient's enrolment in the study. In order to assure maximum safety and control a laminated PLATTRANS Patient Participation Notification Chart was fixed above the patients' beds and Data Collection Forms were added to the patients' end of bed charts.

Platelets for transfusion were ordered by the Haematology team from the Pathology Laboratory and ensured Pathology request for the increment counts one hour and 24-hour post transfusions. Volume per unit, Rh type and platelets' age were documented on the PLATTRANS Data Collection Form for each patient.

All platelet units involved in the study were collected and transfused according to the policy and standard procedure of the LGH, using blood transfusion giving sets with a 170-200 micron filter. Platelet units were collected by nurses and transfused using the randomly assigned transfusion method as determined by the randomization method described above. The electromechanical pumps were set to deliver platelets over 20 minutes, while gravity flow lines were set stat with roller clamp in the fully open position.

Blood samples for platelet increment measurements were performed twice, one hour and 24 hour post platelet transfusion, using a standard technique. Blood collection and sample handling were carried out according to policy and procedure of the LGH using EDTA vacutainers' of 4 ml. Each blood sample was labelled with the patient's name and sent immediately to the National Association Testing Authority (NATA) accredited Pathology laboratory of the LGH. All blood samples were processed in one machine (Beckman Coulter 500, USA). All blood samples were processed within 2 hours of collection.

Sample size calculation

Because there were no data available regarding the differences between the studied different methods of blood transfusion, sample size calculations using data from the first 100 platelet transfusion episodes indicated the need for at least 168 platelet transfusion episodes to detect a minimum mean 20% improvement in platelet count using one of the transfusion pumps compared to gravity transfusion: assuming a mean improvement in the gravity transfusion of 20/nL platelets, a standard deviation of change of 16.8, power 90% and alpha 0.05.

Statistical methods

The 1 hour post-transfusion and 24 hour post-transfusion mean platelet counts in the patients at each separate visit were compared with the pre-transfusion counts, and the differences between the changes using the different transfusion methods were estimated using random effects mixed methods linear regression with unstructured covariance corrected for repeated measures. As the assumptions of linear regression were found to have been violated (significant heteroskedasticity, skewness and kurtosis of residuals using Cameron and Trivedi's decomposition of IM-test, and significant deviation from linearity of response using Ramsey's rest test), P-values were estimated using ordered logistic regression (a non-parametric equivalent of repeated measures ANOVA). All analyses were performed using Stata SE 11.1 (Stata Corp, College Station, Texas USA).

Results

Participant

Between January 2007 and January 2011 at the Launceston General

Gender (Male:Female) ratio	18: 17
Mean Age (range) in years	59 (20-84)
Mean Weight (range) in Kg	75.9 (55-104)
Diagnosis	Number of patients
Acute myeloid Leukaemia	20
Acute Lymphocytic leukaemia	2
Multiple myeloma	4
Aplastic anaemia	2
Malignant Lymphoma	7

Table 1: Description of demographic variables in patients receiving platelet transfusion.

Transfusion technology	Time	N	Mean (SD)	Mean Δ (SD)	Comparison of change			
						Difference	95% CI	P-value2
Gravity	Pre-Tx	45	14.6 (6.9)					
	Post-Tx	45	36.4 (15.6)	21.8 (7.1)				
	24hrs	43	24.4 (13.9)	9.8 (7.3)				
Gemini	Pre-Tx	34	16.0 (5.8)					
	Post-Tx	34	37.7 (12.1)	21.7 (6.8)	Post- vs Pre-	-0.09	(-6.09 to 5.90)	>0.90
	24hrs	34	23.4 (10.3)	7.4 (6.9)	24hrs vs Pre-	-2.44	(-8.34 to 3.46)	0.16
Graseby	Pre-Tx	31	15.4 (5.4)					
	Post-Tx	31	35.8 (11.1)	20.4 (6.4)	Post- vs Pre-	-1.38	(-7.54 to 4.78)	0.77
	24hrs	30	23.0 (11.9)	7.7 (6.4)	24hrs vs Pre-	-2.12	(-8.24 to 3.99)	0.50
Baxter	Pre-Tx	61	12.2 (7.6)					
	Post-Tx	61	37.2 (13.1)	25.0 (6.5)	Post- vs Pre-	3.22	(-1.97 to 8.40)	0.03
	24hrs	61	22.3 (12.5)	10.1 (6.7)	24hrs vs Pre-	0.36	(-4.76 to 5.48)	0.25

Tx= platelets transfusion.
1 Mean platelet count (standard deviation), mean change (Δ) at each separate treatment between pre- and post-treatment and between pre- and 24 hours platelet counts, and differences between those mean changes between the different platelet transfusion technologies; estimates using repeated measures Mean platelet count (standard deviation), mean change (Δ) at each separate treatment between pre- random effects mixed methods linear regression, adjusted for age, gender and initial platelet count. These values are shown for illustration only.
2 The post-estimation checking of the assumptions of linear regression in the above mixed methods linear regression analysis demonstrated significant deviations, so P-values were estimated using ordered logistic regression.

Table 2: Improvement of platelet count immediately post-transfusion and 24 hours after transfusion using three infusion pumps compared to gravity transfusion.

Hospital (LGH), 35 patients were enrolled in the trial (Table 1). The male to female ratio was 18:17 with a mean age of 59 years and mean weight of 75.9 kg. They received a total of 171 platelet transfusions. Forty-five transfusions were performed by gravity flow, 34 using a Gemini pump, 31 using a Graseby pump and 61 using a Baxter pump. Single Donor's platelets as well as pooled platelets were used randomly as determined by availability of these blood products in the blood bank without influence in the trial outcome. The average age of the platelets was four days and platelet-unit volumes ranged from 180 ml to 300 ml. To explore the theoretical influence of pumping action of different mechanical pumps on the transfused platelets, we conducted an ex-vivo platelet infusion testing for all 4 methods used in the trial. We infused a constant amount of platelets with each method in a closed bag system using the same infusion line-set as used for patients. The difference in platelet-reading between pre- and 1 hour post-infusion in each infusion technique did not reveal any significant alteration in both platelet counts for each method.

There were no statistical significant differences based on Rh or ABO group compatibility, age of platelets or patient weight among all studied methods of transfusion.

Primary outcome

In all patients, the mean platelet count before platelet transfusion was 14.0 (SD 6.8), rising to 36.8 (SD 13.5; difference 22.8; 95% CI 20.8 to 24.9; P<0.001) 60 minutes after transfusion, and falling back to 22.6 (SD 11.6; difference 8.6; 95% CI 6.5 to 10.6; P<0.001) 24 hours after transfusion. At 60 minutes the difference of change was similar using the Gemini and Graseby pumps compared to gravity-flow transfusion, but about 15% higher using the Baxter pump (Table 2). At 24 hours the difference of change was similar in all four methods. No severe adverse events occurred.

Discussion

While administration of platelets via a pump offers well-controlled infusion rate, accurate volume measurement and an alarm system for monitoring the infusion, there is no known effect of different pumping devices on the transfused platelets.

It is worth noting that no research has been conducted in adult populations comparing the effect of conventional gravity flow transfusion with these different pumps on platelet increment post transfusion.

The study involves 171 episodes of platelet transfusion with application of a strict exclusion and inclusion criterion. The principle of action of these three devices is very similar; they produce peristaltic movements by multiple mechanical compressions at a constant rate and speed on the plastic tube via which platelets being transfused into the body. Nevertheless, using a simple comparison of the platelet count change from before the transfusion at 24 hours after transfusion, confirms that all studied methods demonstrate similar platelet increment count at 24 hours post platelet transfusion. However, there was a higher platelet increment at 1 hour post platelet transfusion in the Baxter colleague electromechanical pump compared to other methods (p=0.03). The Gemini PC-1 and Graseby 3000 pumps showed similar non-significantly different results from the gravity method in terms of platelets increment 1 hour after transfusion.

It is worth noting that the high variability of the absolute increments in our cohort of patients may influence the statistical significance associated to the Baxter pump in the one hour platelet-increment finding. This difference favouring the Baxter method after one hour of transfusion was not confirmed in the ex-vivo study that using a constant amount of platelets or in the 24 hour platelet increment.

The study compares the outcome of the three electromechanical pumps against the conventional gravity flow method. While Gravity flow method for platelets transfusion by principle of action is the least damaging for platelets, electromechanical pumps on the other hand show considerable near to similar results. Furthermore, the Baxter colleague electromechanical pump's outcome is almost identical to that of the free flow method with a superior result in the 1 hour platelet-increment. Since platelets transfusion via electromechanical pumps show similar increment of the transfused platelets comparing to the conventional free flow method with a high speed rate in this adult population, their use is considered to be justifiable. However, the study is not based to promote any commercial product.

In summary, our study shows that Gravity flow method is

competent as well as efficient. It is also easy to use. Hence, it requires no special training and no regular maintenance. Although a high speed rate of platelets transfusion was essential in our adult study group, it is unlikely to be used in paediatric wards where a precise volume and an accurate rate are required. Therefore, electromechanical pumps that are capable of accurate volume delivery, slower rate speed and automatic alarming system, are crucial in such departments. Furthermore, there was wide variability in the time required for transfusion in the gravity method with an average transfusion rate of 60 minutes versus 20-30 minutes in the electromechanical pump methods.

In conclusion, none of the different infusion pumps was inferior to the gravity flow method indicating that there is a minimal effect on the transfused platelets through the different electromechanical pumps used in this study. The Baxter colleague showed superior results in the immediate 60 minute post transfusion platelet count compared to the gravity flow method (p=0.03). However, this effect was not significant in the next day at the 24 hours platelet count. Furthermore, the free flow gravity method seems to be efficient way for platelet transfusion albeit it cannot provide an accurate control for perfusion rate when required.

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