Platelet transfusion in chemotherapy patients: comparison of the effect of intravenous infusion pumps versus gravity transfusion

ABSTRACT

Platelet concentrates are given to patients suffering with severe thrombocytopenia usually by a gravity transfusion procedure. Increasing patient numbers that are in need of this treatment increase the pressure on hospital staff and space. In order to combat time issues, the use of medical devices such as intravenous infusion pumps are thought to be beneficial for time and simultaneously for safety in transfusion practices. By using infusion pumps, platelet concentrates can be transfused in less time and provide accurate volume measurements. Manufacturers of infusion pumps claim that these devices are safe to be used for blood products including platelet concentrates. However, published studies were performed on older models and newer devices are on the market now. The purpose of this study is to evaluate infusion pumps, which are claimed to be suitable for blood products and to investigate the impact the pumps had on platelets. Furthermore, the study revealed if the intravenous infusion pumps are safe to be used for platelet transfusion as claimed by manufacturers. A simulated transfusion was performed using the Carefusion Alaris GP Plus volumetric pump and Fresenius Kabi Volumat Agilia infusion pump. Samples were taken from expired platelet concentrates before and after passage through the pump. All samples were investigated for full blood count that included platelet count, mean platelet volume (MPV), platelet distribution width (PDW) and a plateletcrit (PCT). The samples were then centrifuged to achieve platelet-poor plasma and then tested for lactate dehydrogenase (LDH). A power calculation performed on the statistical power analysis program G*power indicated a requirement of 82 samples for a power of 80%. Statistical analysis was performed with the IBM SPSS statistic software. A paired sample *t*-test was used to calculate mean, standard deviation and *P* values for the infusion pumps used. The Wilcoxon Signed Rank Test was used to evaluate results that had a non-normal distribution. No statistically significant changes were found for LDH, PDW and platelet count with the Carefusion infusion pump. PCT and MPV were found to have a statistically significant change with *P* values of 0.005 and 0.001, respectively, and showed a decrease in their values. The Fresenius Kabi infusion pump has shown no statistically difference in LDH, platelet count, PCT or PDW, with *P* values of 0.075, 0.425, 0.151 and 0.397, respectively. The MPV showed a statistically significant decrease in its value with a *P* value <0.043. Although only two pumps were tested, the results achieved by testing the devices revealed that there was no influence on the platelet enzyme LDH or the platelet count as the main parameters. However, the findings showed that there was statistically significant differences in MPV of the expired platelet concentrates.

KEY WORDS: Blood platelets.
Infusion pumps.
Markers.
Platelet transfusion.

A. MEESS

Haematology Department, Withybush Hospital, Fishguard Road, Haverfordwest, Pembrokeshire SA61 2PZ

Accepted: 18 June 2015

Introduction

The key function of platelets is building the primary haemostatic plug during haemostasis. They are sensitive blood components and this vital role has to be maintained during platelet transfusion. Patients with reduced platelet counts have an impaired haemostasis and are at risk of bleeding. Thrombocytopenia in chemotherapy patients is often treated with platelet transfusion. In order to combat time issues due to increasing numbers of patients requiring transfusion of blood products and the demand of patient safety, intravenous infusion pumps might be used.

Medical devices do more often replace gravity transfusion for blood components, which also ensure control of infusion rates and infusion time of a blood product.[1–3] All infusion pumps have an alarm system and can discontinue the transfusion automatically if occlusions or air bubbles in the administration system are detected. Infusion pumps are time efficient and ensure increased patient safety.[4–6]

Platelet concentrates have a short shelf life of five days. Platelets are sensitive blood components and have to be stored at 22 (±2) °C. The short life span is due to the storage temperature and the risk of growth of bacteria does restrict the shelf life. However, despite the advantage of using intravenous infusion pumps for platelet transfusion there is concern that these pumps might have a destructive impact on the platelets as they are very sensitive cells, which may cause adverse reactions to the patient receiving the platelet transfusion. All devices have a pumping mechanism that

pumps the fluid by force pressure through the administration. Although known to be safe for the patients as these pumps give alarm for occlusion or air bubbles, the force might cause damage or activate platelets, decreasing the quality of the blood product. There are various stimulants that could cause cell activation that target the platelet and its receptors.[7]

Activated platelets release their content and contribute with a series of activation markers to immune responses and inflammatory processes. β-thromboglobulin is known to be a platelet-specific marker as it is found in platelets only,[7] indicating platelet activation.

Some studies on platelet concentrates have been performed and investigated intravenous infusion pumps. These studies were all performed on very small sample sizes and older devices, which have been replaced by newer models. The literature covering older devices does not indicate any negative effect on platelets and manufacturers' claim that newer models are safe to be used for transfusion of blood products.[8]

Materials and methods

Collection of samples

Samples were taken from expired platelet concentrates which were stored at 22 (±2) °C on a platelet agitator. After the administration set was attached, the pre-transfusion sample was withdrawn by simulating gravity transfusion. The administration set was then applied to its corresponding infusion pump, the Carefusion Alaris GP volumetric infusion pump and the Fresenius Kabi Volumat Agilia infusion pump. The post-transfusion sample was withdrawn by simulating a platelet transfusion with the chosen infusion pumps and samples were collected after passing through the pumping system. The pumps were set up with the recommended flow rate of 500 mL/hour. Samples were collected into native collection tubes without additives.

Testing of samples

After collection, the samples were then taken for investigation of full blood count (FBC) to obtain platelet indices such as platelet count, mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW). The FBC was performed on the Beckman Coulter LH 750 analyser.

Platelets were analysed and determined by the Coulter principle in the red cell bath. Platelets were considered if the volume was 2–20 fL. The values were then used in the platelet histogram in order to give values for MPV and PDW. The PCT was calculated by the analyser's computer system according to a formula supplied by Beckman Coulter.

The samples were then spun at ambient temperature for 10 min at 3000 rpm in a Thermo Electron B4i multifunction centrifuge. One aliquot was used for lactate dehydrogenase (LDH) testing, performed on the Ortho Clinical Diagnostics Vitros 5.1 FS analyser.

The Vitros analyser used the principle of the slide method. The slides containing pyruvate and NADH were the analytical element with underlying layers in one cartridge where one drop of sample was applied. The LDH enzyme from the sample catalysed pyruvate and NADH to lactate and NAD^+. The amount of oxidation was equal to LDH activity.

Additional aliquots were stored at –30°C for further tests such as enzyme immunosorbent assay (ELISA) of β-thromboglobulin.

Intravenous Infusion pumps

The infusion pumps assessed in this study were the Carefusion Alaris GP volumetric pump and the Fresenius Kabi Volumat Agilia infusion pump. The administration set for the Carefusion pump was the Blood set u/v spike R/C 2 x SmartSite Y-ports (1 before filter) 200 micron filter Roll/C Alaris safety clamp L270cm P/31ml 3mm id. Fresenius Kabi recommended the VL TR00 set for transfusion blood bags for the Volumat Agilia infusion pump. Both pumps were volumetric pumps that move the blood product components through the infusion system by applying negative pressure.

Statistical analysis

The statistical analysis was performed using IBM SPSS statistics software (version 21). A Kolmogorov-Smirnov test was carried out to test for normal distribution of the results. Differences of data with normal distribution were determined by Student's paired *t*-tests, and data with non-normal distribution were evaluated with the Wilcoxon Signed Rank Test. The statistical significance between pre- and post-transfusion samples was determined and $P<0.05$ were considered statistically significant.

Results

Samples were taken over a course of 12 weeks. There was no statistically significant change in LDH or PDW. LDH has shown no statistically significant change from pre-infusion (mean=431 [SD= 149]) to post-infusion device (mean=428 [SD=143], t –1.287, $P=0.202$, 95% confidence interval [CI] –1.52–7.1). The η^2 statistic (0.02) indicated a small effect size. PDW showed no statistically significant change from pre-transfusion (mean=17.9 [SD=0.516]) to post-transfusion (mean=17.9 [SD=0.512], t–0.04, $P=0.97$, 95% CI –0.059–0.057). The η^2 statistic (0.00) indicated a very small effect size.

There was a statistically significant decrease in PCT from pre-transfusion (mean=0.733 [SD= 0.221]) to post-transfusion testing (mean=0.723 [SD=0.215], $t[83]=2.87$, $P=0.005$, 95% CI 0.003– 0.016). The η^2 statistic (0.09) indicated a medium effect size.

Carefusion Alaris infusion pump

The results obtained from the Carefusion Alaris pump revealed that the data were not normal and therefore the non-parametric alternative to the *t*-test, the Wilcoxon Signed Rank Test, was performed to reveal statistics on MPV and platelet count. A statistically significant decrease was found in the volume of platelets using the Carefusion infusion pump ($z= –4.237$, $P<0.001$, $r=0.32$). The median score on MPV decreased from pre-transfusion (8.3) to post-transfusion (8.2).

The platelet count did not show statistically significant change in the Wilcoxon Signed Rank Test ($z= –1.54$, $P=0.124$, $r=0.01$). The median score increased from 835 to 856, while the 25th and 75th percentiles decreased from 677 to 662 and 1105 to 1077, respectively.

Fresenius Kabi infusion pump

A paired sample *t*-test was performed to evaluate the Fresenius infusion pump and its impact on LDH, platelet count and PCT. LDH showed no statistically significant change from pre-transfusion (mean=861 [SD=366]) to post-transfusion device (mean=857 [SD=368], $t[86]=1.802$, $P=0.075$, 95% CI –0.451–9.17. The η^2 statistic (0.036) indicated a small effect size.

There was no statistically significant change in the platelet count from pre-transfusion (mean=694 [SD=226]) to post-transfusion testing (mean=690 [SD=223], $t[85]=0.801$, $P=0.325$, 95% CI –5.687–13.358). The η^2 statistic (0.007) indicated a small effect size.

The PCT also did not show a statistically significant change in the paired sample *t*-test, from pre-transfusion (mean=0.585, [SD=0.189]) to post-transfusion (mean=0.579 [SD=0.185], $t[84]1.449$, $P=0.151$, 95% CI –0.002–0.014). The η^2 statistic (0.024) indicated a small effect size.

The non-parametric Wilcoxon Signed Rank Test was performed to give statistical results on the non-normal values of MPV and PDW. Regarding MPV, the test revealed a statistically significant decrease in the volume of platelets ($z=2.028$, $P<0.05$) with a small effect size ($r=0.15$). The median score decreased from pre-transfusion (median= 8.7) to post-transfusion (median=8.5). The Wilcoxon Signed Rank Test indicated no statistically significant change for PDW ($z=–0.847$, $P=0.397$) with a small effect size ($r=0.06$). The median score decreased from pre-transfusion (17.9) to post-transfusion (17.7), while the 25th percentile did not change and the 75th percentile decreased from pre-transfusion (median=18.7) to post-transfusion (median=18.6).

Discussion

The study was performed to evaluate newer models of intravenous infusion devices currently on the market and claimed by manufacturers to be suitable for transfusion of blood products. The pumps were tested for platelet concentrates only and by simulating platelet transfusion. The primary objective was to detect major or minor impact of the infusion pumps to the platelet as a cell. The secondary objective was if there was an impact of the pumps, how distinctive it would be and how the quality of the platelet would be affected. There are no newer studies published on larger sample sizes, which had included the two infusion devices and laboratory tests performed.

Both pumps did not have any influence on LDH or platelet counts. The platelets were moved by shear force through the administration set and the infusion pumps. There was no damaging impact on the cytosol of the cells, which could have lead to a leakage of LDH into the plasma and therefore an increase of LDH or decrease in cell count. The values of LDH as well as the platelet count demonstrated no change between pre-transfusion and post-transfusion samples.

Statistical results of this study demonstrated that transfusions via medical devices such as the Carefusion Alaris GP volumetric pump did contribute to a decreased level of MPV and PCT, and the Fresenius Kabi Volumat Agilia infusion pump had an influence on the level of PCT. The MPV presented the volume of the platelets and its decrease indicated a change in platelet morphology. The study revealed that the shear force arising from the pumping mechanism of the infusion pumps might have an influence to the shape of the platelet. Changes in platelet volume can indicate changes in platelet function.[9] A study performed by Maxwell *et al*.[10] concluded that signalling processes trigger shape changes in platelets, and these changes are shear-dependent. Some platelets change from flat discs to spherical cells. This change left the platelet appearing smaller in size, which would explain the decrease of MPV.

The Carefusion pump has been shown to trigger a decrease in PCT which is a calculated value and results from the multiplication of platelet count and MPV, as an index of total platelet mass. Associated with the MPV value, the PCT will follow the direction of MPV in its decrease. It is not a parameter used for diagnostic purposes, but for research use only.

Values for LDH, platelet count and PDW stayed constant and where not affected by the Carefusion infusion pump, although it would be of interest to know the actual activation status of the cell. MPV or PCT do not give any information about the actual stage of activation of a platelet, or if the cell is close to releasing its contents or close to apoptosis. There are certain laboratory tests available as activation markers, such as β-thromboglobulin, that would give information about this state.

Gravity transfusion is the safer method for platelet transfusion compared to transfusion via medical devices but it has disadvantages in terms of time planning and efficiency. It is also the more cost-efficient method as specific administration sets have to be used with infusion pumps, which raise the costs for consumables. Gravity transfusion has the least damaging impact on the platelets, and staff need no further training. There is no time-consuming maintenance of medical devices involved that would lead to extended clerical work.

Intravenous infusion pumps are the more expensive choice for transfusion. Appropriate trained healthcare professionals are needed to use these medical devices, although all staff involved with administration of any blood component require specific training and competence assessment. However, the occlusion alarms contribute to the safe use of infusion pumps. The patient does not need to be constantly monitored during the treatment and staff may focus on other important tasks.

Owing to the large sample size needed and the restricted availability of expired platelet units, some concentrates were used more than once in this project, but were attached with a new administration set every time a sample was withdrawn. This procedure allowed the sample size needed for this study to be achieved.

An aliquot of all samples was stored for further testing. β-thromboglobulin as a platelet-specific protein would have been a very useful parameter to investigate any platelet activation that may have taken place. Another test considered was the pfa 100 (Sysmex/Siemens), which evaluates platelet function under shear force; however, this equipment was unavailable.

It can be concluded that the infusion pumps tested are suitable for platelet transfusions. However, certain rules must be considered in order to comply with local rules and regulations regarding transfusion of blood products. All staff must be aware of any medical device alerts, and the pumps

should be used for their designed purpose only and within recommended guidelines. Furthermore, it is not advisable to increase recommended speed or pressure for certain blood products.

Use of intravenous infusion pumps can contribute to more efficient transfusion and patient management. Despite higher costs in training and consumables, the use of intravenous infusion pumps could contribute to reducing costs for expensive platelet concentrate special deliveries to rural hospitals. A small number of studies have considered infusion devices for platelet transfusion and have reported suitability for this use, but every pump should be considered and evaluated locally. □

Thanks are due to Dr Mary Ward and Dr George McKerr, University of Ulster, Coleraine Campus, Northern Ireland, for their help, support and guidance; Dr Sandra Frances Sweetman for valuable advice on statistics; Mrs Helena Tollick (senior biomedical scientist); Mr Ted Allen (chief biomedical scientist); and all staff from the haematology and biochemistry department, and Mr Peter Stace (Lead Nurse, Procurement) during the setting up and conduct of this work.

References

1 Fischer-Nielsen A, Stissing T, Maansson C, Joergensen BG. Pressure-aided transfusion of platelets: does it affect the platelets? *Transfusion* 2010; **50** (2): 361–5.

2 Norville R, Hinds P, Wilimas J, Fairclough D, Fischi S, Kunkel K. The effects of infusion methods on platelet count, morphology, and corrected count increment in children with cancer: *in vitro* and *in vivo* studies. *Oncol Nurs Forum* 1994; **21** (10): 1669–73.

3 Wagner B, Wuest TH, Beeser H. Effects of an infusion pump with peristaltic mechanism of action on various blood components *in vitro* (in German). *Beitr Infusionsther* 1992: **30**: 454–9.

4 Khalafallah A, Al-Barzan AM, Camino A *et al*. An open-labelled, randomized cross-over study of the effect of electromechanical pumps versus conventional gravity flow on platelet transfusion in adult haematology patients. *Transfus Med Hemother* 2013; **40** (1): 22–6.

5 Snyder EL, Ferri PM, Smith EO, Ezekowitz MD. Use of an electromechanical infusion pump for transfusion of platelet concentrates. *Transfusion* 1984; **24** (6): 524–7.

6 Snyder EL, Rinder HM, Napychank P. *In vitro* and *in vivo* evaluation of platelet transfusions administered through an electromechanical infusion pump. *Am J Clin Pathol* 1990; **94** (1): 77–80.

7 Kamath S, Blann A, Lip G. Platelet activation: assessment and quantification. *Eur Heart J* 2001; **22** (17): 1561–71.

8 Lieshout-Krikke RW, van der Meer PF, Koopman MM, de Korte D. Effect on the quality of blood components after simulated blood transfusions using volumetric infusion pumps. *Transfusion* 2011; **51** (8): 1835–9.

9 Leader A, Pereg D, Lishner M. Are platelet volume indices of clinical use? A multidisciplinary review. *Ann Med* 2012; **44** (8): 805–16.

10 Maxwell MJ, Dopheide SM, Turner SJ, Jackson SP. Shear induces a unique series of morphological changes in translocating platelets: effects of morphology on translocation dynamics. *Arterioscler Thromb Vasc Biol* 2006; **26** (3): 663–9.