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Re-evaluating the shelf-life of whole blood for use in trauma: impact of storage on platelet function.

Sian Huish¹, Laura Green ^{2, 3}, Carly Kempster⁴, Peter Smethurst¹, Michael Wiltshire¹, Lucy Bower¹, Jennifer Jolley¹, Marie Anne Balanant¹, Lubosz Lewandowski¹, Emily Horner⁵, Rebecca Cardigan^{* 1, 6}

¹NHS Blood and Transplant, Cambridge, ²NHS Blood and Transplant, ³Barts Health Trust, London, ⁴University of Reading, Reading, ⁵Imperial College, London, ⁶University of Cambridge, Cambridge, United Kingdom

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Abstract Content: Background: There is an immense interest in using Whole Blood (WB) transfusion for early resuscitation of trauma patients with major bleeding in the pre-hospital setting. The shelf-life of WB component (21-35 days depending on jurisdiction) was established decades ago, primarily based on the viability of red cells. This study aimed to determine the platelet function of leucocyte-depleted WB (LD-WB) over storage in order to re-establish the shelf life.

Methods: LD-WB was prepared using a platelet-sparing LD filter (Terumo WB-SP Imuflex). LD-WB was held at 2 - 6 °C alongside comparator arms consisting of: A) UK standard pooled buffy coat platelets stored at 20 - 24 °C (RT-PLTS) B) pooled platelets held at 2 - 6 °C (COLD PLTS) and C) platelet rich plasma (PRP) produced using the Terumo Imuflex WB-SP kit, for 21 days. A series of *in vitro* assays were assessed.

Results: There were fundamental changes in the platelet function of LD-WB over storage at 2 - 6 °C for 21 days. Platelet count was retained to a mean of 57 ± 14 % of starting number at day 21 in 80 % of LD-WB components compared with 97 ± 2 % at end of shelf life (day 7) in RT-PLTS. Over time the platelets in LD-WB become more activated, as seen in increased CD62P expression (Day $1 - 7 \pm 3.7$ % vs. Day $21 - 59 \pm 17.1$ %) and annexin V binding (Day $1 - 2 \pm 0.2$ % vs. Day $21 - 21 \pm 15.1$ %). For comparison, 18.6 ± 6 % of platelets in RT-PLTS demonstrated CD62P expression at day 7 whilst Annexin V binding in RT-PLTS at day 7 was 2.6 ± 0.5 %. LD-WB demonstrated decreased response to agonists over time (CD62P expression with **ADP**: (Day $1 - 73 \pm 9$ %, Day $21: 13 \pm 8$ %), **TRAP-6:** (Day $1 - 80 \pm 6$ %, Day $21 - 13 \pm 8$ %), **CRP-XL:** (Day $1 - 64 \pm 15$ %, Day $21 - 11 \pm 12$ %). From day 12 onwards, LD-WB showed very little ability to aggregate in response to ADP and TRAP-6. Platelet-derived microparticles increased steadily throughout storage, which corresponded with increased potential to promote thrombin generation (Day $1 - 72 \pm 5.7$ s to clot vs. Day $21 - 38 \pm 3.5$ s to clot) in LD-WB. Metabolism was higher in RT-PLTS than cold-stored components.

Conclusion: During storage of LD-WB, there is a substantial loss of platelet count, coupled with progressive loss of aggregatory response, and increased activation. These data, along with previously published work to understand red cell function and plasma quality in LD-WB *in vitro* and international experience, were used to recommend a shelf life of 14 days for LD-WB in the UK. This work is part of ongoing collaborative efforts to establish the clinical need and feasibility of WB in the treatment of major haemorrhage, particularly in the pre-hospital environment.

Disclosure of Interest: None Declared