

Letter by Lin et al Regarding Article, “Nitric Oxide Scavenging of Red Blood Cell Microparticles and Cell-Free Hemoglobin as a Mechanism for the Red Cell Storage Lesion”

To the Editor:

We congratulate Donadee et al¹ on a very elegant and thorough study on the mechanism of vasoconstriction mediated by transfusion of red blood cells containing low amounts of hemolyzed cells and microparticles via nitric oxide (NO) scavenging and the Editor for bringing an important issue of quality of red blood cells used for treatment of a large number of patients in need of transfusion to the attention of clinicians outside traditional transfusion medicine practice. These results provide new fundamental insights into NO signaling during endothelial cell injury and vascular impairment as a result of red blood cell storage lesions. Standard blood banking conditions can produce free hemoglobin (at or below 10 $\mu\text{mol/L}$) and microparticles that can react with NO 1000 times faster than intact erythrocytes, producing an increased mean arterial blood pressure suggestive of a vasoconstriction response.

However, an increase in mean arterial blood pressure in rats infused with stored blood plasma is only an indication, but not direct evidence of, vasoconstriction. Methods such as isolated vessel perfusion (coupled with tension transducer) or laser-Doppler flowmetry (measurement of regional blood flow) are more precise measurements in determining vasoconstriction. Additionally, this study could have been enhanced with an addition of a NO scavenger concurrent to infusing stored blood plasma (ie, 2-(4-carboxyphenyl)-4,4,5,5-tetramethylimidazoline-1-oxyl-3-oxide derivative)² of human red blood cells. The comparison of red cell plasma or oxyhemoglobin infusion in the presence or absence of a NO scavenger would ensure that all of the remaining NO is scavenged and have minimum to no effect on vascular tone. This critical step would also ensure that all of the NO byproducts, such as nitrates and nitrites, cannot regenerate and form NO in the normoxic state.³

The vasoconstriction produced by impaired NO bioavailability and generation of potential reactive oxygen species during reinfusion of blood can be reduced by recent advances in anaerobic storage of blood. Improving the quality and efficacy of stored red blood cells can be achieved by removing <93% of oxygen in stored blood, which results in enhanced ATP levels protecting ATP-mediated NO bioavailability and reduced oxidative damage protecting protein thiols that may be critical in NO signaling in vivo.⁴ This method allows for storage of red blood cells longer than the standard time

limit of 6 weeks.⁵ Nevertheless, the study performed by Donadee et al definitely provides critical mechanistic insights into the fundamentals of endothelial cell injury and vascular impairment of red cell storage lesions. Emerging novel concepts of prolonging blood storage and preventing red cell storage lesions will be highly beneficial for improved clinical outcomes of a vast variety of critically ill patients and those in need of blood transfusions.

Disclosures

Dr Yoshida is an employee of New Health Sciences. New Health Sciences Inc holds an exclusive license to the anaerobic blood storage technology.

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