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401.BLOOD TRANSFUSION

Loss of Oxygen Transport Potency As a Function of RBC Storage Duration

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BACKROUND: Red blood cell (RBC) oxygen (O_2) capture/release is regulated via homeostatic modulation of hemoglobin oxygen (Hb-O_2) affinity in a manner that stabilizes O_2 delivery in the setting of reduced O_2 availability (i.e., hypoxia, anemia) or increased O_2 consumption (i.e., exercise, stress, disease). This is achieved via production of allosteric effectors (i.e., 2,3 DPG, ATP) and adjustment of the RBC biochemical milieu (i.e., pH, anion concentration) in response to regional stimuli including temperature and carbon dioxide (CO_2) abundance, encountered during circulatory transit (aka Bohr effect). Blood storage is known to affect Hb-O_2 affinity, because the environment to which the RBCs are exposed affects cellular metabolism, influencing [allosteric effector], pH, and [anion]. In addition, key proteins may either become depleted or impaired during storage, including anion exchange-1 (AE-1 or Band 3) and carbonic anhydrase, the two proteins that enable the Bohr effect. We therefore explored the novel hypothesis that RBC oxygen transport potency is diminished as a function of blood storage duration, due to loss of the Bohr effect.

METHODS: Fresh (healthy control) or stored RBCs units (leuko-reduced in AS-1; Impact Life Davenport IA, USA), were analyzed weekly for up to 42 days. Hb-O_2 affinity was determined from the oxygen dissociation curve (ODC), which describes the relationship between the partial pressure of oxygen (pO_2) and the fraction of oxyhemoglobin ($FHbO_2$). ODCs were constructed at 2 fixed pH values (HEMOX analyzer, TSC Scientific Corp, PA, USA) or 2 fixed CO_2 levels (thin film rotating tonometer; Meon, Graz, Austria, in conjunction with a gas blender; Oxystreamer, Biospherix, Parish, NY, USA, with samples measured by arterial blood gas machine; ABL90Flex, Radiometer, Brea, CA, USA). Analysis included (1) standard p50 determination (i.e., pO_2 at which Hb is 50% saturated with O_2), (2) delta p50 between ODCs at fixed pH 7.6 and 7.2 - HEMOX, or ODCs at fixed pCO_2, eucarbia ~40 mmHg and hypercarbia ~70 mmHg - tonometer), (3) Area between the two curves measured (ABC), as described above. Additional analyses were performed from ODC data, including comparison of blood **O_2 content per gram Hb (with SO_2 converted to blood O_2 content assuming 1-gram Hb binds 1.34 ml O_2), and blood** O_2 capacitance ($\beta O2$), which quantifies the amount of O_2 unloaded for a given arteriovenous pO_2 gradient.

RESULTS: As a function of blood storage duration, we found significant (1) reduction in p50 at 2 fixed pHs (HEMOX) and 2 fixed pCO_2s (tonometer) (2) reduction in delta p50 between ODCs at fixed pH 7.6 and 7.2 (HEMOX), or fixed pCO_2; eucarbia ~40 mmHg and hypercarbia ~70 mmHg (tonometer), i.e., significantly reduced Bohr effect (3) reduction in the area between ODC curves at different pH or CO_2 levels (ABC), a more comprehensive representation of the Bohr effect, across the full range of pO_2s encountered during circulatory transit (rather than the single point p50 measurement), (4) reduction in blood oxygen content per gram Hb, and (5) reduction in $\beta O2$.

SUMMARY: We demonstrate that blood storage significantly impairs the Bohr effect. Consequently, compared to fresh RBCs, the oxygen transport potency of stored RBCs in AS-1 within one week is ~50-60% that of fresh RBCs and by the time the unit is outdated, is down to ~35%. Consequently, 2.86 the number of RBCs from an expiring stored transfusion unit are required to move the same amount of O_2 as a similar number of RBCs in fresh blood.

Disclosures No relevant conflicts of interest to declare.

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