Abstract

Red cell 2,3-DPG and ATP levels decline rather rapidly during storage which result in poor oxygen offloading ability and post-transfusion viability respectively of such cells. Since the steady-state levels of these metabolites are determined by the relative activities of the key enzymes of glycolysis (phosphofructokinase and pyruvate kinase) and 2,3-DPG by-pass (2,3-diphosphoglycerate mutase/phosphatase), we reasoned that it may be feasible to maintain near-normal levels of 2,3-DPG and ATP by manipulating, i.e. activating or inhibiting, the activities of these enzymes using their physiological effectors either singly or in combination. Since pyruvate kinase is most strategically located in glycolysis with regard to 2,3-DPG and ATP metabolism, we first elected to investigate the effects of inhibiting the enzyme during red cell storage. In this study, we first prove the validity of the proposed concept by demonstrating that red cells from individuals heterozygous-deficient for pyruvate kinase maintain higher than normal levels of both 2,3-DPG and ATP. Moreover, we demonstrate that L-alanine and L-phenylalanine, the known inhibitors of pyruvate kinase maintain higher 2,3-DPG and ATP levels throughout the five-week storage period. These results thus further confirm the scientific validity of the proposed concept and provide a means of improving the quality and/or shelf-life of stored red cells.

PMID: 3593307