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CARBON MONOXIDE BOUND RED BLOOD CELLS PREVENT ALTERATION OF HEPATIC CYTOCHROME P450 ACTIVITY AFTER HEMORRHAGIC SHOCK AND RESUSCITATION

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ABSTRACT

The resuscitation from hemorrhagic shock induces systemic ischemia/reperfusion (I/R) injury. Recently, it was found that cytochrome P450 (CYP) was degraded during I/R. Since carbon monoxide (CO) exhibited the effect of heme stabilization, we investigated whether exogenously administered CO could prevent an alteration of hepatic CYP activity in hemorrhagic shock and resuscitation. Here, we used red blood cells (RBC) as a CO carrier (CO-RBC) for resuscitation. Hemorrhagic shock rat was made by withdrawing 40% of blood, and the rat was resuscitated with isovolumic RBC or CO-RBC. At 1 hr after resuscitation, protein expressions of hepatic CYP isoforms (CYP1A2, 2C11, 2E1 and 3A2) were significantly decreased in RBC group as compared to normal group, whereas these expressions were maintained in CO-RBC treatment. Furthermore, we conducted the pharmacokinetic study of dapsone, which is a multiple CYP substrate. The AUC of dapsone in RBC group was markedly increased as compared to normal group, while that in CO-RBC group was little changed. The present study suggested that resuscitation by RBC induces pharmacokinetic alterations of CYP metabolized drugs, whereas these unfavorable actions are minimized by CO-RBC resuscitation.