LECTURE

Physiological Effects of Modified Hemoglobin As an Oxygen-carrying Macromolecule

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Abstract. A stabilized hemoglobin as oxygen-carrying macromolecules was developed. It had approximately 90,000 dalton molecular weights and its intravascular half life was 36 hours. Its molecular size was less than 0.1 μm. Its hemoglobin concentration was 6% and P_{50} value was 24 mmHg. The oxygen carried inside the plasma performs differently than the oxygen carried inside the red cells. Only less than 0.3 ml of oxygen in 100 ml of blood is available inside the plasma while 14–19 ml of oxygen is carried inside the red cells. Thus, less than 5 ml of oxygen is available inside the plasma of the entire body. When a patient develops hypovolemic shock, the red cells are bypassed and are not perfused directly inside the tissues. However, the plasma should reach such hypoxic tissues. Thus, infusion of oxygen-carrying macromolecules in the plasma should be therapeutically effective even if less than 100 ml of stabilized hemoglobin solution were infused under shock conditions. The basic physiology of oxygen-carrying macromolecules is described in detail, which is different from the oxygen carried inside the red cells. (Keio J Med 48 (1): 38–43, March 1999)

Key words: oxygen-carrying macromolecules, oxygen in plasma, blood transfusion, artificial blood, blood substitute

As a possible replacement for red blood cells, fluorocarbon emulsion[1–4] was experimentally employed during the early 1970s. Although fluorocarbon emulsion was demonstrated as an effective oxygen carrier in experimental animals and a minimal number of toxic effects was demonstrated in acute phase studies, its long-term effects were questionable. One year after injecting this chemical preparation, there were subsequent physiological effects due to chronic tissue reactions to this resident fluorocarbon polymer: a slowly developed and persistent anemia, leukocytosis, and fever, followed by death due to chemical pneumonitis. A paper on the injected fluorocarbon particles that remained inside the body for an extended period of time, particularly inside the lung tissues, failed to be published. The reason this paper was rejected was claimed to be because it employed a barbaric experimental method of total body melting of the dogs by HCl. Even though it was claimed that the fluorocarbons should be expirated into a gaseous form together with the respiratory air, at least two-thirds of the injected fluorocarbon particles were entrapped, primarily in the lung tissues and recovered after all animal tissues were dissolved.

It was speculated that the injected polymer particles were immediately covered with plasma proteins. The particle sizes were increased and the gas exchange properties of the fluorocarbon emulsion were impaired. Subsequent entrapment inside the capillaries should have occurred. Chronic tissue reactions occurred slowly and resulted in clinical pictures of chemical pneumonities. The natural sequence of these phenomena *in vivo* should have been realized at that time. Unfortunately, over a quarter century ago, knowledge on blood and tissue compatibility with foreign body particles was very limited. Much progress has been made since that time. Eliminating or reducing these strong body defense mechanisms against these man-made oxygen-

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