

Food Deprivation and Glucose Homeostasis in Hemorrhagic Stress

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Abstract

Although *malnutrition* has been associated with increased morbidity and mortality after surgery, little attention has been focused on the effect of *short term food deprivation* on responses to stress. It is known that already 24h of food withdrawal depletes hepatic carbohydrate reserves, and alters glucose production from glycogenolysis to gluconeogenesis. These changes may alter the potential of supplying sufficient glucose during stress. Therefore, the effect of short term food deprivation for glucose homeostasis in stress has been investigated. Fed or 24h food deprived rats were subjected to hemorrhagic hypotension, and glucose kinetics were studied in relation to hepatic glycogen content, endocrine response and fluid homeostasis. Survival after standardized hemorrhage was also compared.

Fed rats developed massive hyperglycemia during hemorrhage, while after 24h food deprivation, this response was absent, due to lack of hepatic glycogen reserve. Associated with hyperglycemia during hemorrhage was the development of hyperosmolality and increased plasma refill. The endocrine response to hemorrhage was different in fed compared to food deprived rats. Corticosterone levels increased substantially during stress in food deprived rats, while this response was absent in fed rats. Adrenalin and glucagon increments were marked and similar in both groups. Insulin levels were unchanged during hemorrhage in food deprived animals, while the response in fed rats was attenuated. Opposite developments were found for somatostatin during bleeding in the two groups; an early peak was noted in fed rats, and thereafter somatostatin levels declined. In food deprived animals, levels of somatostatin successfully increased.

Despite massive hyperglycemia and hyperinsulinemia in fed rats during bleeding, glucose uptake was only moderately increased, implying the development of insulin resistance during hemorrhagic stress. Both fed and food deprived animals increased glucose recycling during hemorrhagic stress, indicating increased gluconeogenesis. However, the results obtained indicate that total gluconeogenesis was greater in fed compared to food deprived rats. During the period after hemorrhage, glucose levels were normalized in fed rats, and simultaneously hepatic glycogen content was substantially increased. During this period, persistent hyperinsulinemia was recorded. Adrenalin levels declined rapidly, while reduction in glucagon was slower. Notably, despite the normalization in glucose levels, the fluid mobilized during early hemorrhage was retained within the circulation.

Twenty four hour food deprivation prior to standardized hemorrhage was associated with significant mortality, while all fed animals survived. Induction of hyperglycemia by hypertonic glucose infusion in food deprived rats during hemorrhage improved survival. It is concluded that food deprivation 24h, in the rat, greatly influences not only responses to hemorrhagic stress, but results in significantly increased post-hemorrhage mortality. The changes observed were all related to glucose homeostasis.